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MEDICAL TIMES

Landmark in Cancer Research
Hepatitis • Rabies
Aureomycin

Medical Book News
Contemporary Progress

Editorials
Contents Pages 7a, 9a

Vol. 77 **November 1949** **No. 11**

The Journal of General Practice

a **new**
antibacterial
agent . . .

Wide antibacterial activity, low toxicity and virtual elimination of renal complications distinguish the use of Gantrisin* 'Roche', a new and remarkably soluble sulfonamide. Highly effective in urinary as well as systemic infections, Gantrisin does not require alkali therapy because it is soluble even in mildly acid urine. More than 20 articles in the recent literature attest its high therapeutic value and the low incidence of side-effects. Gantrisin is now available in 0.5 Gm tablets, as a syrup, and in ampuls. Additional information on request.

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Gantrisin®

* *Brand of sulfisoxazole (3,4-dimethyl-5-sulfanilamido-isoxazole)*

'Roche'

RUTAMINAL*

the
protection
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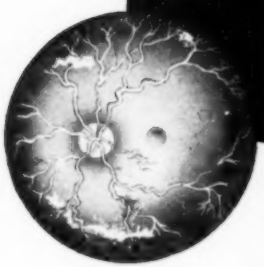
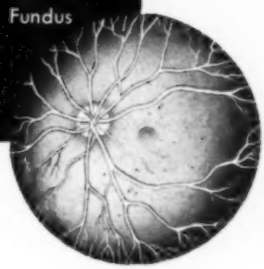
rutin
the
action
of
aminophylline
the
sedation
of
phenobarbital
—for
use
in
selected
cardiovascular
and
diabetic
conditions
in
which
excessive
capillary
fragility
presents
a
complicating
hazard
—bottles
of
100
tablets

Ocular Fundus in Degenerative Vascular Disease—Hypertension, Diabetes, Arteriosclerosis —note tortuous blood vessels, areas of exudation, hemorrhagic areas.



Normal Ocular Fundus

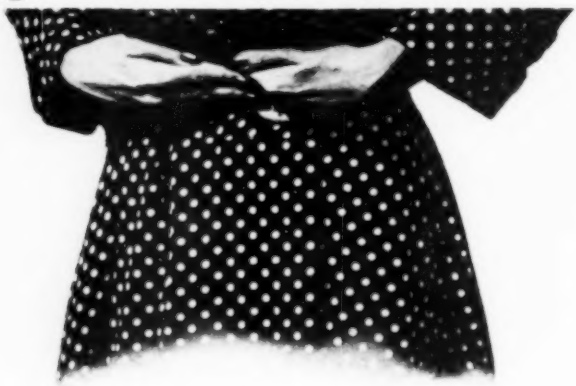


*RUTAMINAL is the trademark of Schenley Laboratories, Inc. and designates exclusively its brand of tablets containing rutin, aminophylline, and phenobarbital.

schenley laboratories, inc., 350 fifth ave., new york 1, n. y.

TRASENTINE-PHENOBARBITAL

a powerful antispasmodic . . . with selective action avoiding undesirable side effects



Effective relief of visceral spasm is generally obtained with Trasentine or Trasentine-Phenobarbital. By its selective action, Trasentine avoids the undesirable side effects of dryness of the mouth and pupillary dilatation frequently produced by belladonna or atropine. These advantages have caused physicians to prescribe more Trasentine and Trasentine-Phenobarbital than probably any other brand of antispasmodic.

● Average adult dose is one or two tablets 3 or 4 times daily as required.

TRASENTINE-PHENOBARBITAL – Tablets (yellow) contain 50 mg. Trasentine hydrochloride with 20 mg. phenobarbital, in packages of 100 and 500.

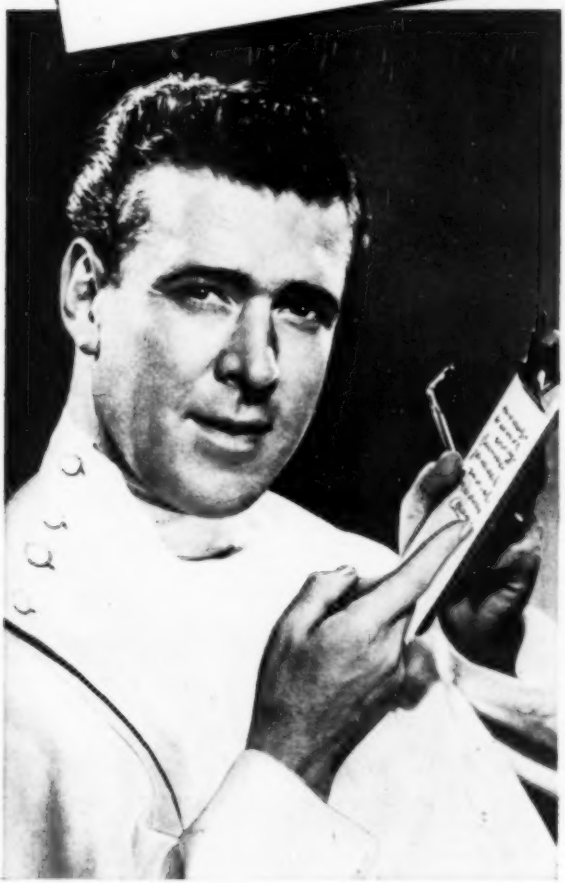
TRASENTINE – Tablets (white) of 75 mg., in bottles of 100 and 500; also suppositories of 100 mg., and ampuls of 50 mg.

Ciba PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY

TRASENTINE (brand of adiphenine)—Trade Mark Reg. U. S. Pat. Off. 2/1431M

THROAT SPECIALISTS REPORT ON 30-DAY TEST OF CAMEL SMOKERS—

"Not one single case of throat irritation due to smoking CAMELS!"



YES, these were the findings in a total of 2,470 weekly examinations of hundreds of men and women from coast-to-coast who smoked only Camels for 30 consecutive days! And the smokers in this test averaged one to two packages of Camels a day!

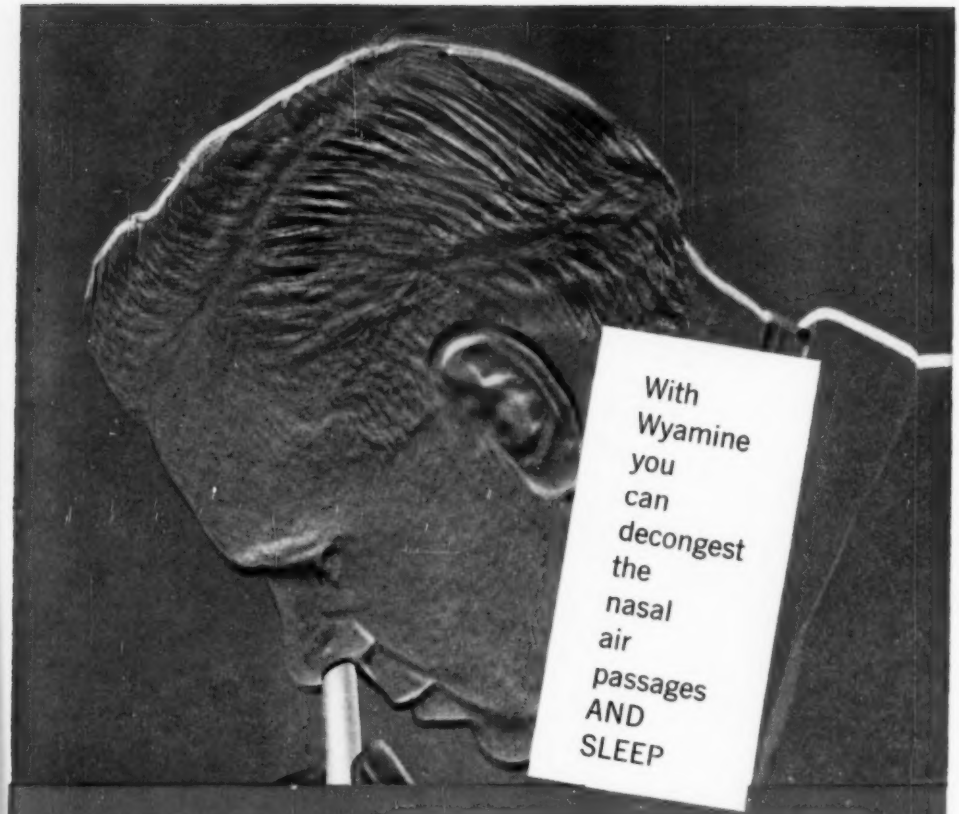
According to a Nationwide survey:

MORE DOCTORS SMOKE CAMELS

than any other cigarette!

Doctors smoke for pleasure, too! When three leading independent research organizations asked 113,597 doctors what cigarette they smoked, the brand named most was Camel!

R. J. Reynolds Tob. Co., Winston-Salem, N. C.



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**N-methylphenyl-tertiary butylamine*

WYAMINE, either as the volatile base or the water-soluble sulfate, is an effective new vasoconstrictor, possessing several important advantages. It produces a local vasoconstriction approximately equal to that of ephedrine, but its action is very rarely attended by returgescence, or by nervousness, excitability or insomnia.

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WYAMINE INHALER

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SOLUTION WYAMINE SULFATE

SOLUTION WYAMINE-TYROTHRICIN

Use with dropper or **JETOMIZER®**

Wyeth®

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Contents

Contents

call it

dermatophytosis pedis
epidermophytosis
tinea pedis
dermatomycosis
trichophytosis
or *"athlete's foot"*

then treat it with

'Timofax'
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undecylenate
ointment

'Timofax' Ointment makes possible more efficient management of "athlete's foot". It has proved to be remarkably effective—while affording the blandness essential for prolonged prophylaxis and treatment.

Chemically related to the normal constituents of sweat, undecylenic acid does not break down the skin in the manner of a foreign substance. Hopkins et al. state that "The high percentage of effectiveness and low incidence of irritation indicated that undecylenic acid was the best of the fungicides tested for routine treatment of sub-acute cases." *(J. Invest. Dermat., 7:239, 1946)*

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BRAND
undecylenate
ointment

'Timofax' contains undecylenic acid 10% as free acid and potassium undecylenate in a scented vanishing cream base. Supplied in ¾ oz. collapsible tubes.

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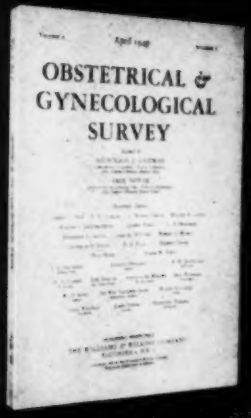
Medical Book News



"... these statistics are the best that have been reported. In fact, they couldn't be any better."

Editor: Obstetrical & Gynecological Survey
Vol. 4, No. 2: April, 1949: page 190

...tistics refer... are those reported by Dr. ... W. Smith in her article, "Diethyl... stilbestrol in the Prevention and Treatment ... of Complications of Pregnancy", in the Novem... ber, 1948, issue of *The American Journal of Obstetrics and Gynecology*. This study of 632 pregnancies showed that, "under stilbestrol treatment the habitual aborter enjoys the same outlook for a living baby as does the average gravida. This is what I mean by saying that these statistics are the best that have been reported".[1]

This report affords additional evidence that the treatment of threatened and habitual abortions with des — Grant Process diethylstilbestrol — as pioneered by Karl John Karnaky[2], is the most effective treatment available.

The work of Silbernagel and Burt[3], and of Rosenblum and Melinkoff[4] showed that with diethylstilbestrol *68.4% more* cases were carried to term than with progesterone. In fact, it is now felt that the administration of progesterone may actually hasten abortion[5].

des is the only diethylstilbestrol prepared by the unique Grant Process of triple crystallization. Highly micronized des tablets are dissolved within a few seconds and are uniformly absorbed into the blood stream. des is specifically designed for the treatment of threatened abortion, habitual abortion and premature labor. The living results obtained with des are the best that have been reported. "In fact, they couldn't possibly be any better."

des IS BEST

REFERENCES
1. Editor: Obs. and Gyn. Survey. 56. 821-834. Nov. 1948. 2. Karnaky, K. J. Estrogenic Tolerance in Pregnant Women. Amer. Jr. Obs. and Gyn. 53. 312-316. 1947. 3. Silbernagel, W. M. and Burt, O. P. Ohio State Med. Jr. 39. 430 May 1943. 4. Rosenblum and Melinkoff. Preservation of the Threatened Pregnancy with Particular Reference to the Use of Diethylstilbestrol. West. Jr. Surg. Obs. and Gyn. 55. 597-603. Nov. 1947. 5. Hamblen, E. C. Endocrinology of Woman. Springfield, Ill. Charles E. Thomas. 1948. p. 476.

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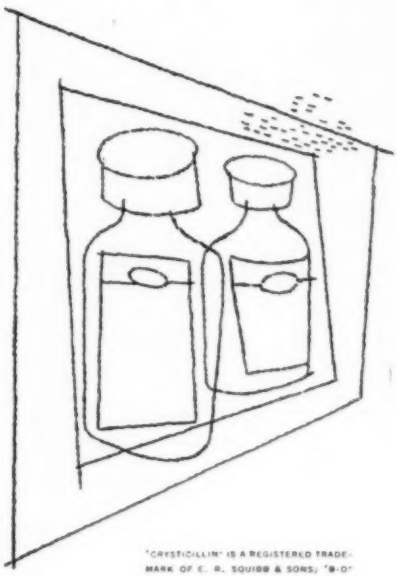
SUPPLIED IN MULTIPLE DOSE VIALS, 1,500,000 and 3,000,000 units; also in 300,000 unit B-D cartridge with *disposable* syringe.



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(contains 10% N-ethyl-o-crotonotoluide)

scabicidal non-irritating antipruritic bacteriostatic

Clinical experience has demonstrated that a single application of EURAX cream completely eradicates scabies in more than 88 per cent of cases. Two applications, 24 hours apart, produce cure-rates up to 100 per cent.[1-6]

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No preliminary scrubbing necessary.

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BIBLIOGRAPHY: 1. Couperus, M.: J. Invest. Dermat. *13*:35, 1949. 2. Tronstein, A. J.: Ohio State M. J., *in press*. 3. Goldman, L.: Connecticut M. *J. 13*:624, 1949. 4. Patterson, R. L.: Work in progress. 5. Domenjoz, R.: Schweiz. med. Wchnschr. *76*:1210, 1946. 6. Burckhardt, W., and Rymarowicz, R.: Schweiz. med. Wchnschr. *76*:1213, 1946.

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The world wide Geigy organization—established in Switzerland in 1764—has a noteworthy history in the production of synthetic organic compounds which have found wide acceptance as chemicals of highest quality. Leadership in organic research and synthesis have led naturally to the development of original pharmaceuticals now widely prescribed in virtually every country of the world.

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In a comparison of 12 commonly used antibacterial agents for eye infections

SODIUM SULFACETIMIDE SOLUTION 30%

(SODIUM SULAMYD®)

was found best.[1]

It is "an ideal antiseptic in cases of acute and chronic infection of the conjunctiva."[1] Among 3000 eyes treated "there were no reactions which could be considered either as a sensitivity or as an allergic reaction."[1]

In blepharitis, SODIUM SULFACETIMIDE OPHTHALMIC OINTMENT 10% is indicated since only "an ointment could be expected to maintain an effective concentration of the drug."[2]

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1. Mayer, L. L.: Arch. Ophth. 39:232, 1948.
2. Thygeson, P., in discussion on Mayer, L. L.: Arch. Ophth. 39:232, 1948.

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SODIUM SULFACETIMIDE SOLUTION 30%

An Emulsion of Mineral Oil and Irish Moss

(1) **Kondremul Plain—when regularity is to be obtained and maintained through softening of the feces by a colloidal emulsion of microscopically fine particles which are stable, indigestible, unabsorbable and which mix intimately with the fecal mass—non-irritating, non-habit-forming.**
Dosage: **Adults, one tablespoonful; children, one dessertspoonful.**

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At last a beautiful diaphragm, a snow white article of perfection that your patients will admire.

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Lighter in weight,
Pure white in color,
Of more uniform thinness,
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Daintier in appearance,
Easy to use.

Your Ortho representative will show it to you on his next visit.

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POTENT TREATMENT *for* SPASMS OF SMOOTH MUSCLE

NOVATRIN* with PHENOBARBITAL performs the dual function of a potent antispasmodic and a sedative. Each tablet contains 1/4 grain phenobarbital and 1/12 grain of Novatrin (homatropine methylbromide) which, by depressing the vagal and parasympathetic nerve terminals, will produce an antispasmodic effect comparable to that of 1/25 to 1/50 grain of atropine sulfate. But the toxicity of Novatrin is only about one-thirtieth that of atropine so that undesirable side effects, such as dryness of the mouth and blurring of vision, are extremely unlikely to occur. Novatrin with Phenobarbital is recommended when nervous tension or emotional strain complicate and aggravate spasms of smooth muscle and, in general, when other forms of antispasmodic therapy fail to produce a satisfactory response. *Specifically recommended in —*

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BILIARY AND RENAL COLIC
PEPTIC ULCER AND PYLOROSPASM
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Novatrin WITH *Phenobarbital*

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Sodium Penicillin G

by Tongue, by Lung, by G. I. Tract

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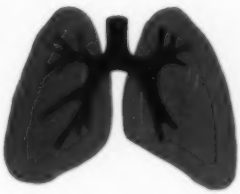
Sublingual PENALEV tablets (50,000 or 100,000 units) are rapidly absorbed, quickly create therapeutic penicillin blood levels.



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Potent penicillin G aerosol solutions can be prepared readily by dissolving PENALEV tablets in water or normal saline.

By G. I. Tract:

PENALEV tablets dissolve promptly and completely in milk, fruit juices, or infant formulas, without appreciably changing their tastes.

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Soluble tablets sodium penicillin G: 50,000 and 100,000 units; vials of 12 tablets crystalline. Sharp & Dohme, Philadelphia 1, Pa.

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SHARP & DOHME

Soluble Tablets Crystalline

Sodium Penicillin G

LETTERS

TO THE EDITOR

This department is offered as an Open Forum for the discussion of topical medical issues. All letters must be signed. However, to protect the identity of writers, who are invited to comment on controversial subjects, names will be omitted when requested.

FEE SPLITTING

"I wish I could share the sentiments of Dr. R. B. in your June issue regarding fee splitting. In this state of undignified professional fee splitting our legislature has passed legislation, now in force, prohibiting doctors from splitting fees under penalty of fines. Pray for us!"

H.A.L., M.D.
Tacoma, Washington

NATIONAL HEALTH INSURANCE

"Seated here in my sun parlor with the restful view of the Inlet to Gardiner's Bay only a 3-minute walk from my front door, I came across the *August 1928* number of the MEDICAL TIMES. A confrère of our 'once great' profession had just been commenting on my article that you had asked me to write—asking me what I 'thought of things *now?*' With it was a comparatively recent letter of yours, asking me to comment as 'a personal favor' (as you kindly put it) in your 'Letters' column. Then I wrote as 'the only physician member of the State Senate.' If you *now* want to allude to the 100 per cent cooperation I then received from many of your readers in rectifying the abuses to which I called their attention, you may state that *never* was the call more crucial than now. Without a shadow of a question, our profession, yours and mine, stands on the brink of socialization. Our United States cannot countenance Political Medicine. *In Union there is strength.*"

William Lathrop Love, M.D.
East Hampton, L. I.

—Continued on page 28a

NOW—

Council Accepted

Protinal Powder—
the whole protein.

Delicious — tastes more like a confection than a pharmaceutical preparation.

Micro pulverized — mixes far more readily with milk or other foods than do ordinary granule preparations.

Effective — high protein content (61.25%) supplies all of the amino acids known to be necessary to maintain life and growth in a 100% digestible form.

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TIME FOR *Thantis* LOZENGES

For throat irritations 'Thantis'* Lozenges provide effective relief. 'Thantis' Lozenges are especially beneficial in soothing these conditions because they are both antiseptic and anesthetic for mucous membranes of the throat and mouth. These effects are due to the two active medicinal agents, 'Merodicein'* an antiseptic of low toxicity, and Saligenin, a mild local anesthetic. When 'Thantis' Lozenges are dissolved in the mouth, the two ingredients dissolve slowly, providing prolonged medication of the throat.

Each lozenge contains 'Merodicein' (H. W. & D. brand of monohydroxymercuridiiodoresorcinsulfonphthalein-sodium) 1/8 grain, Saligenin (orthohydroxybenzyl-alcohol, H. W. & D.) 1 grain.

Supplied in vials of 12 lozenges in individual cartons packed in dozens.

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MORE AND MORE...

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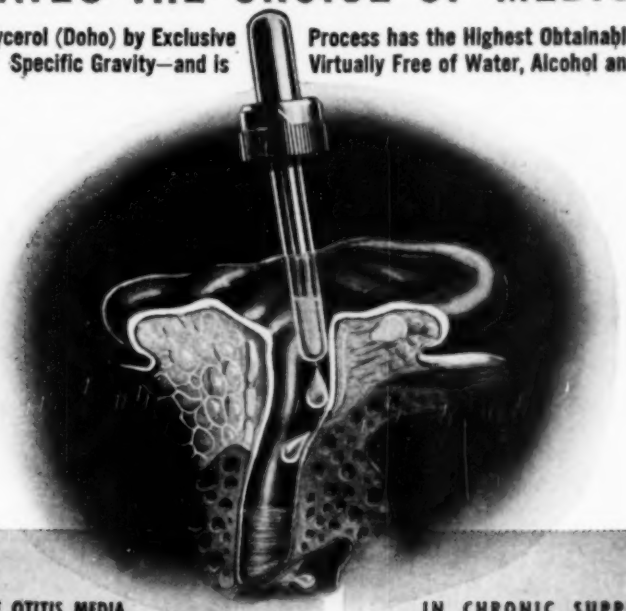

IN ACUTE OTITIS MEDIA

REMOVAL OF IMPACTED CERUMEN

AS AN ADJUNCT TO SYSTEMIC ANTI-INFECTIVE THERAPY, AS PENICILLIN, ETC.

CONTAGIOUS DISEASE EAR INVOLVEMENTS

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...because its potent decongestant, dehydrating and analgesic action provides quick, efficient relief of pain and inflammation in any intact drum involvement.

FORMULA:

Glycerol (DOHO)	17.9 GRAMS
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Antipyrine	0.81 GRAMS
Benzocaine	0.21 GRAMS

IN CHRONIC SUPPURATIVE OTITIS MEDIA, FURUNCULOSIS AND AURAL DERMATOMYCOSIS

USE

O-TOS-MO-SAN

...a potent chemical combination *(not a mere mixture)*, combining Sulfathiazole and Urea in AURALGAN Glycerol (DOHO) Base—because it exerts a powerful solvent action on protein matter, liquefies and dissolves exuberant granulation tissue, cleanses and deodorizes, and tends to exhilarate normal tissue healing in the effective control of chronic suppurative otitis media.

FORMULA:

Urea	2.0 GRAMS
Sulfathiazole	1.6 GRAMS
Glycerol (DOHO) Base	16.4 GRAMS

Literature and samples sent to physicians on request.

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LETTERS

continued

FERTILITY "PLUS"

"The specialists and the 'country doctors' do not know too much about fertility—many of us know too much about the fertility of the un-married females!

"Many years ago a couple came to see me very anxious to procreate. The wife told me of the various patent and proprietary remedies that she had taken orally and the various specialists that she had consulted. Husband had all the tests and proven fertile. Wife had 2 or 3 D & C's.

"In desperation she asked what she could do to have a baby. Facetiously, I answered, 'Change bulls.' After thirty-six she either took my advice—or the changed acidity of flora allowed her to have one."

J. F. N., M. D.
St. Pauls, N. C.

REFRESHER ARTICLES

"I think it is an excellent idea to summarize and condense the newest known therapeutics of a certain medical entity."

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New York, N. Y.

LIKE MT

"I have been receiving MEDICAL TIMES for the past six months and I have enjoyed reading it very much. I find it very useful as a 'refresher' and I think it does fill a real want of the busy physician who is entirely unable to read the many journals that come to his office."

E. R. Zemp, M.D.
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CAUBREN® COMPOUND

cold combatant

containing:

Chlorothen Citrate	—25 mg	long-acting antihistaminic of low toxicity
Acetophenetidin	—320 mg	analgetic and antipyretic synergists
Caffeine	—32 mg	analgetic and antipyretic synergists

caubren compound curbs colds by

- ***relieving symptoms***
- ***shortening duration***
- ***reducing contagion***

administration: *One to two tablets every 3-4 hours for at least 48 hours beginning as soon as possible after appearance of initial symptoms.*

available: *Bottles of 100 tablets*

Whittier

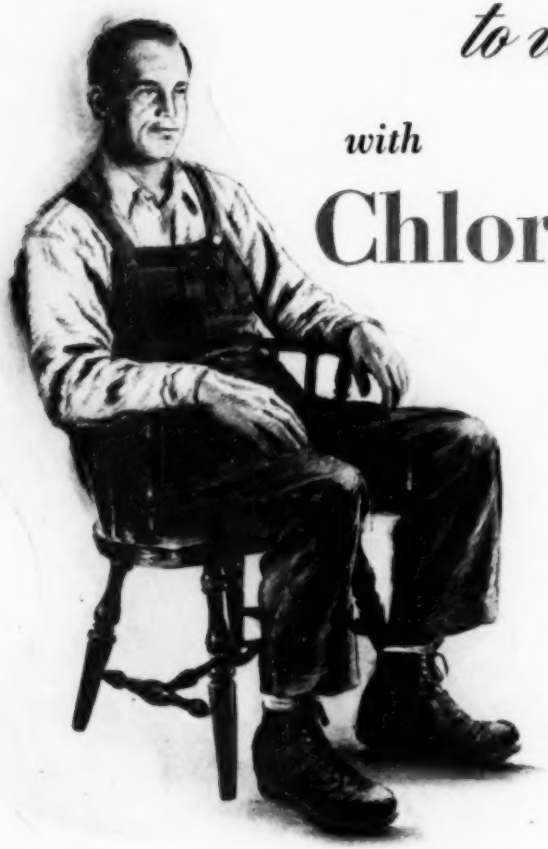
LABORATORIES • DIVISION NUTRITION RESEARCH LABORATORIES, CHICAGO 30, ILLINOIS

combat common colds with Caubren Compound!

He'll be back to work sooner...

with

Chloromycetin®



The cost of medication, of course, is but one item in the total cost of illness, the greatest expense stemming from the length of incapacitation and consequent loss of working time. One distinct advantage of CHLOROMYCETIN therapy is its fundamental economy—quick clinical response, reduced morbidity, shortened convalescence and earlier return of the patient to his job.

Particularly dramatic results are now obtained in a disease such as typhoid fever, where the illness formerly ran its course for several weeks because of the lack of specific therapy. The lengthy hospitalization, special nursing care, the supportive measures during this prolonged period—all have contributed to increased costs. However, CHLOROMYCETIN changes this: the duration of illness is greatly reduced, defervescence occurring within 2 to 3 days after treatment is begun. With control of the infection, general improvement is manifest and recovery is rapid.

The high degree of efficacy of CHLOROMYCETIN has also been demonstrated in a number of other diseases previously unresponsive or poorly responsive to treatment, such as acute undulant fever, urinary tract infection, typhus fever, Rocky Mountain spotted fever, scrub typhus, and granuloma inguinale.

PACKAGING

CHLOROMYCETIN (Chloramphenicol, Parke-Davis) is supplied in 0.25 Gm. Kapseals. Descriptive literature on CHLOROMYCETIN is available to physicians on request.

PARKE, DAVIS & COMPANY

DETROIT 32, MICHIGAN

MEDICAMENTA VERA · PD & CO.

"...what precious drops are these"

Shakespeare

TWO PRODUCTS OF OPTIMUM ACCEPTABILITY

OL-VITUM Drops. For a highly palatable multi-vitamin dietary supplement, that is completely dispersible in food or any aqueous fluid, Ol-Vitum Drops are meeting a gratifyingly high professional acceptance. Like all IVC products, they are found to be CLINICALLY ECONOMICAL.

Each cc contains:

Vitamin A	10,000 USP Units	Vitamin B_6	1.6 milligrams
Vitamin D	2,000 USP Units	Niacin Amide	15 milligrams
Vitamin B_1	3 milligrams	Natural Mixed Tocopherols	3 milligrams (Equivalent to 2.25 milligrams alpha Tocopherol Acetate)
Vitamin B_2	0.8 milligrams		
Vitamin C	100 milligrams		

AD-VITUM Drops. In vitamin therapy or dietary supplementation where high potency of the A-D combination alone is indicated, Ad-Vitum Drops are especially desirable. Like its companion product, Ad-Vitum Drops are palatable, will mix with food or any aqueous fluid and again are CLINICALLY ECONOMICAL.

Distilled Vitamin A Ester, Viosterol in Oil, Sorbitan Fatty Acid Ester derivative, Vegetable Oil and Glycerin in a flavored aqueous vehicle.

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ULTRACAIN® OINTMENT offers prompt and prolonged relief in pruritus, ulcers, fissures, lacerations, abrasions, burns and in mucocutaneous lesions.

It is significantly free from allergizing side-effects.

To meet increasing prescription demands, stock ULTRACAIN OINTMENT today. Order 1-oz. tubes with applicators and 1-lb. jars from your service wholesaler.

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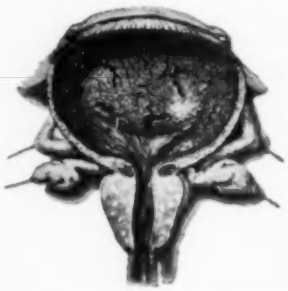
PATIENT under TREATMENT

ENJOYS

Gratifying Relief

from distressing

URINARY SYMPTOMS



Distressing symptoms of urinary tract infection such as urinary frequency, pain and burning on urination can be relieved promptly in a high percentage of patients through the simple procedure of administering Pyridium orally.

With this easy-to-administer and *safe* urinary analgesic, physicians can often provide their patients with almost immediate relief from distressing urinary symptoms during the time that other therapeutic measures are directed toward alleviating the underlying condition.

Pyridium is virtually nontoxic in therapeutic dosage and can be administered concomitantly with streptomycin, penicillin, sulfonamides, or other specific therapy.

The complete story of Pyridium and its clinical use is available on request.

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Manufacturing Chemists

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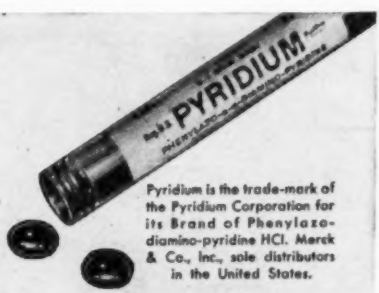

Pyridium is the trade-mark of the Pyridium Corporation for its Brand of Phenylazo-diamino-pyridine HCl. Merck & Co., Inc., sole distributors in the United States.

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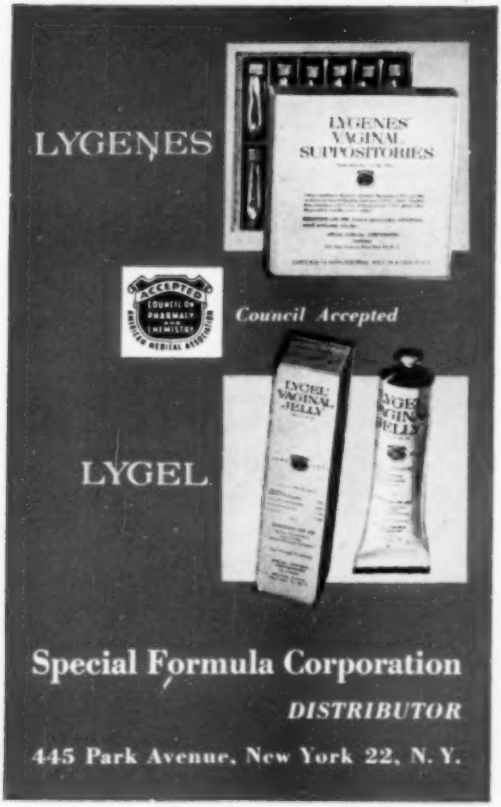
Contraceptive Products provide clinically proved protection

Normal function without anxiety, fear or devices—plus patient-cooperation.

The aim of modern contraception—to instill complete confidence—is fully realized in this line of contraceptives which provide a high degree of effectiveness. Non-toxic, esthetically acceptable, non-irritating, economical.



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Hydroxyquinoline Benzoate 0.30%
p-Chloro-symm.-m-dimethylhydroxybenzene 0.05%
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Zinc Sulfocarbolate 0.50%
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LYGEL VAGINAL JELLY—A jelly of high spermicidal efficacy with freedom from irritation and ready patient-acceptance. Readily dispersible. Does not lose viscosity at body temperature. 3-oz. tubes.

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p-tert. Amylhydroxybenzene 0.05%
Benzalkonium Chloride 0.10%
Lactic Acid 0.25%
pH 3.4

Literature and clinical trial packages on request.

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'WARNER'

an anticoagulant preparation with prolonged action for the prevention and treatment of thromboembolic disorders.

HEPARIN/PITKIN MENSTRUUM 'Warner' is a safe and clinically established means of providing prolonged anticoagulation action in the body.

One subcutaneous injection of HEPARIN/PITKIN MENSTRUUM 'Warner' is usually sufficient to increase the blood coagulation time for a period of 24 to 48 hours . . . without the necessity for the cumbersome, discomforting and time-consuming procedures usually required when maintaining blood fluidity in thromboembolic disease.

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'WARNER'

is available in 200-mg and 300-mg ampuls for subcutaneous injection, cartons of 6 ampuls each, with or without vasoconstrictors.

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fewer: **stillbirths**
neonatal deaths
complications of delivery
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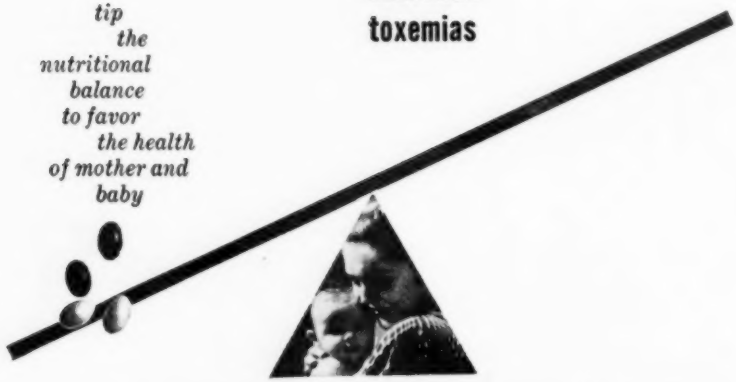
tip the nutritional balance to favor the health of mother and baby



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. . . specially designed to help meet increased vitamin-mineral needs during pregnancy and lactation. Improved maternal nutrition means better physical health for the mother with many prenatal symptoms and discomforts almost wholly relieved or avoided, and sturdier babies with greater resistance to disease.

Two vitamin (dark color) capsules provide: vitamin A 10,000 units, thiamine 5 mg., riboflavin 5 mg., niacinamide 20 mg., choline 50 mg., pyridoxine 1 mg., pantothenic acid equiv. 10 mg., ascorbic acid 150 mg., vitamin D 1000 units, d, alpha-tocopherol 5 mg., and B complex factors from 400 mg. yeast.

Two mineral (light color) capsules provide: calcium 220 mg. (from di-calcium phosphate 750 mg.), iron 50 mg. (from ferric phosphate 3 gr.), phosphorus 200 mg., magnesium 1.5 mg., copper 1.5 mg., manganese 1.0 mg., iodine 0.1 mg., and zinc 1.0 mg.

professional samples and literature upon request.

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RAY-TROTE
IMPROVED

a 'step-down transformer' for the management of hypertension

An *increased dose* of chemically standardized, *physiologically active* veratrum viride distinguishes the new RAY-TROTE IMPROVED CAPSULES . . . by *Raymer*. Three effective vasodilators—nitroglycerin, sodium nitrite, and veratrum viride—are combined in the green capsule. A mildly sedative dose of phenobarbital in the formula helps to maintain lowered blood pressure levels. Based on a formula used by physicians for nearly a quarter of a century . . . now made even more effective. Prescribe it in your next case of hypertension.

*Formula: Phenobarbital . . . ¼ grain; Sodium Nitrite . . . ½ grain; Nitroglycerin . . . 1/250 grain; Potassium Nitrate . . . 1 grain; with equivalent of Veratrum Viride Tincture (containing 0.1% alkaloids) . . . 4 minims; Crataegus Fluidextract . . . 1 minim.

*Also available . . . for the hypertensive patient with capillary fault . . . **RAY-TROTE WITH RUTIN** . . . representing the same formula with 20 mgm. rutin added. Supplied in two tone (green and yellow) capsule.

Sample and literature sent on request.
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Over a Quarter Century Serving Physicians

Modern MEDICINALS

Physicians will find that these brief resumes of essential information relative to the newer products are so prepared that they may be removed and pasted on standard 3x5" file cards, and filed as illustrated in the adjoining picture, for ready reference.

Coricidin

11-49

MANUFACTURER: Schering Corporation, Bloomfield, N. J.

INDICATIONS: Indicated at the onset of the first symptoms of a common cold, as sneezing, dryness of the throat, etc. Therapy may abort a cold at its inception or modify the cold favorably if instituted within a few hours after initial symptoms appear.

ACTIVE CONSTITUENTS: Each tablet contains Chlor-Trimeton maleate 2.0 mg. (1/30 gr.) acetylsalicylic acid 0.23 Gm. (3.5 gr.), acetophenetidin 0.15 Gm. (2.5 gr.), and caffeine 0.03 Gm. (0.5 gr.).

DOSAGE: Two tablets with onset symptoms, followed by 1 tablet every 3 hours for 1 to 2 days.

HOW SUPPLIED: In vials of 12 tablets and bottles of 100 and 1000 tablets.

Diffusin

11-49

MANUFACTURER: Ortho Pharmaceutical Corp., Raritan, New Jersey.

INDICATIONS: Useful in reducing the pain, induration, and length of time of administration commonly associated with hypodermoclysis. With local anesthetics Diffusin speeds the diffusion of the anesthetics and the area and depth of anesthesia. Nerve block anesthesia can be induced more promptly and completely. Diffusin is also an excellent aid to infiltration anesthesia procedures. Additional applications of this new and unique drug are currently under investigation.

ACTIVE CONSTITUENTS: Highly purified lyophilized hyaluronidase.

DOSAGE: As indicated.

HOW SUPPLIED: In packages of three vials, each vial containing 150 T.R.U. (turbidity reducing units) of sterile, lyophilized Diffusin.

Penicillin Powder Inhaler

11-49

MANUFACTURER: Schenley Laboratories, Inc., 350 Fifth Ave., New York, N. Y.

INDICATIONS: For oral or nasal inhalation.

ACTIVE CONSTITUENT: Each cartridge contains 100,000 units crystalline penicillin G potassium.

DOSAGE: Delivery of the penicillin powder is accomplished by the patient inhaling slowly and deeply, removing inhaler from mouth or nostril during exhalation, repeating the process until the cartridge is empty.

HOW SUPPLIED: In a glass bottle containing 3 cartridges of 1,000 units each. A plastic nozzle fits into the cartridge.

—Continued on page 44a

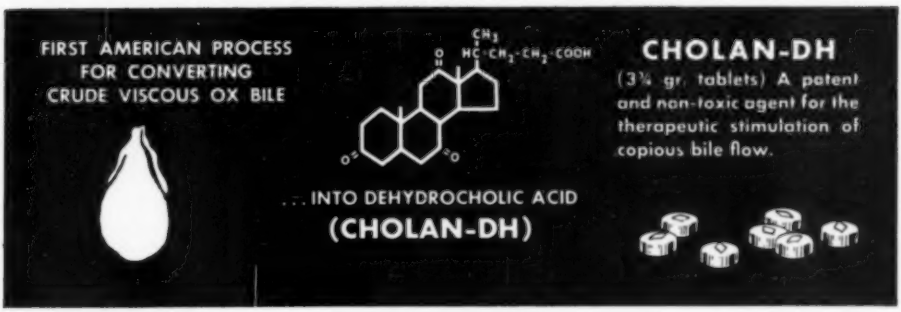
FOR THE MEDICAL MANAGEMENT
of BILIARY DISEASE

Cholan-DH

Dehydrocholic Acid 3¾ gr.

CHOLAN-DH IS DEHYDROCHOLIC ACID PREPARED IN THE MALTBIE LABORATORIES BY THE EXCLUSIVE MALTBIE PROCESS.

Through its potent hydrocholeretic action, Cholan-DH counteracts the tendency to stasis of bile. It affects a drainage of the biliary ducts, establishing a freely flowing current which encourages the removal of mucus, inspissated bile, bacteria and their toxic products. It also discourages the ascent of infection.



SUPPLIED IN BOTTLES OF 100, 500 AND 1000 TABLETS.

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So much better that we have discontinued 'Benzedrine' Inhaler

Physicians tell us that they and their patients find BENZEDREX INHALER the best inhaler they have ever used. The active ingredient of BENZEDREX INHALER is 1-cyclohexyl-2-methylaminopropane, a new S.K.F. compound. It has exactly the same agreeable odor as Benzedrine*, gives even more effective and prolonged shrinkage, and does NOT produce excitation or wakefulness.

We are sure you will find that BENZEDREX INHALER is the best volatile vasoconstrictor you have ever used.

Smith, Kline & French Laboratories, Philadelphia

Each BENZEDREX INHALER is packed with 1-cyclohexyl-2-methylaminopropane, S.K.F., 250 mg.; and aromatics.

*"Benzedrine" (racemic amphetamine, S.K.F.) and 'Benzedrex' T.M. Reg. U.S. Pat. Off.

FOR BALANCED MANAGEMENT IN

essential hypertension

STABILIZATION of blood pressure (*Maxitate*).

TREATMENT and **PROPHYLAXIS** where capillary fragility is a complicating factor or a threat (*Rutin*).

STRENGTHENING of intercellular cement (*Ascorbic Acid*).

SEDATION where needed (*Phenobarbital*).

Maxitate with Rhamnotin and Maxitate with Rhamnobarb are rational and effective therapeutic agents in providing tranquility and a sense of well-being to the hypertensive.

MAXITATE® with RHAMNOTIN

Each GREEN tablet contains:

*Maxitate	30 mg.
Rutin	15 mg.
Ascorbic Acid	20 mg.

MAXITATE® with RHAMNOBARB

Each ORANGE tablet contains:

*Maxitate	30 mg.
Rutin	15 mg.
Ascorbic Acid	20 mg.
Phenobarbital	15 mg.

**Mannitol Hexanitrate Stabilized by Strasenburgh Research*

MAXITATE® with RHAMNOTIN

MAXITATE® with RHAMNOBARB

R. J. STRASENBURGH Co.

PHARMACEUTICAL CHEMISTS SINCE 1886

ROCHESTER 4, NEW YORK

Write today for literature and complimentary samples.

Thephorin Lotion

11-49

MANUFACTURER: Hoffmann-La Roche, Inc., Roche Park, Nutley 10, N. J.

INDICATIONS: Highly effective in relieving allergic skin disorders, pruritic complaints, sunburn and insect bites. Thephorin Lotion is particularly useful for patients with dry skin.

ACTIVE CONSTITUENT: Contains 5 per cent Thephorin, highly effective antihistamine, in a pleasantly scented, flesh-colored lotion.

DOSAGE: Applied to the affected area as often as necessary for the relief of symptoms. From one to six applications daily are usually adequate.

HOW SUPPLIED: In 2-oz and 16-oz bottles.

Thalinol-MRT

11-49

MANUFACTURER: Marvin R. Thompson, Inc., 67 Greenwich Ave., Stamford, Conn.

INDICATIONS: In the treatment of functional or atonic constipation due to various causes. Because of the relatively slow release of the active agent, phenolphthalein U.S.P., from the special base, action tends to be gentle though firm and uniform, stools are generally of normal consistency with less griping.

ACTIVE CONSTITUENTS: Each capsule contains 5 grains phenolphthalein U.S.P.

DOSAGE: One capsule when needed for relief of temporary or occasional constipation as prescribed by a physician.

HOW SUPPLIED: In bottles of 30 and 100.

Mercuhydrin with Ascorbic Acid

11-49

MANUFACTURER: Lakeside Laboratories, Inc., Milwaukee 1, Wisconsin.

INDICATIONS: May be used alone in some instances for maintenance therapy but generally will serve best as a supplement to parenteral administration. With parenteral administration, the new oral Mercuhydrin permits reduction in the number of injections and longer intervals between treatments. For the ambulant cardiac, oral diuretic therapy is of decided advantage to both the patient and the physician. Its use facilitates the frequent-dosage schedules of modern diuretic therapy.

DOSAGE: As indicated.

Cogenat

11-49

MANUFACTURER: The National Drug Company, Philadelphia 44, Pa.

INDICATIONS: Cogenat is effective in the treatment of estrogenic deficiencies occurring at the menopause; in senile vaginitis; functional uterine hemorrhage; postpartum breast engorgement; female hypogenitalism; amenorrhea; in the male, palliation of local discomforts from prostatic carcinoma and its metastases may be obtained.

ACTIVE CONSTITUENT: A potent and well-tolerated estrogen.

DOSAGE: 1.25 mg. to 3.75 mg. daily. Since response to estrogenic therapy varies widely, fixed dosage schedules are impractical. Following initial relief of symptoms a maintenance dosage just sufficient to provide continued relief is recommended.

HOW SUPPLIED: Cogenat Tablets (Green)-0.625 mg., and (Orange)-1.25 mg., in bottles of 100 and 1000.

What do you demand in a toxoid, Doctor?

small dosage volume?

purity?

concentrated potency?

high antigenicity?

Of course, doctor, you want the best possible combination of these advantages.

Research and manufacturing know-how of CUTTER, first producer of combined toxoids, have developed in their *new* purified toxoids products which meet all of your demands.

As an example, consider the superiority of the *new*, purified **DIP-PERT-TET***—for simultaneous immunization against diphtheria, pertussis, and tetanus:

1. **Immunization routine** *is simplified with three injections of 0.5cc each at monthly intervals.*

2. **Purified toxoids** *assure virtual freedom from reactions due to bacterial protein components.*

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When single immunizations are indicated or booster shots are required, there is a PURIFIED TOXOID–CUTTER–available in both single and multiple dose packages. Your pharmacist has them in stock.

*__DIP-PERT-TET__—*Cutter's diphtheria and tetanus toxoids and pertussis vaccine combined for simultaneous immunization against diphtheria, pertussis, and tetanus.*

**__Alhydrox__—*Trade name for aluminum alhydrox adsorption, exclusive with CUTTER.*

CUTTER

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To the *Gravida* whose child was born alive and well, and to you the Physician who prescribed fetus-saving *des* — *Bio-des* in cases of habitual abortion, threatened abortion and premature labor, we respectfully dedicate this space.

Frank L. Haley, B.S., M.D.
Research Medical Director
Grant Chemical Co., Inc.
95 Madison Avenue
New York 16, N. Y.

Some Facts on

ERTRON®

STEROID COMPLEX—WHITTIER

—and Conclusions

1. FACT In combined series of 1,020 arthritic patients treated with Ertron, good results were obtained in 38.5%, fair results in 43.7% and poor results in 17.8%. Thus 82.2% of patients showed significant improvement. In addition, there were quickly evident heightened well being, increased strength and weight gain.

Conclusion The therapeutic effects of Ertron are not limited to the local manifestations of rheumatoid arthritis. The action is systemic, like the disease itself. Rapid alleviation of joint pain and stiffness along with improvement in the general condition make Ertron a valuable feature in the management of rheumatoid arthritis.

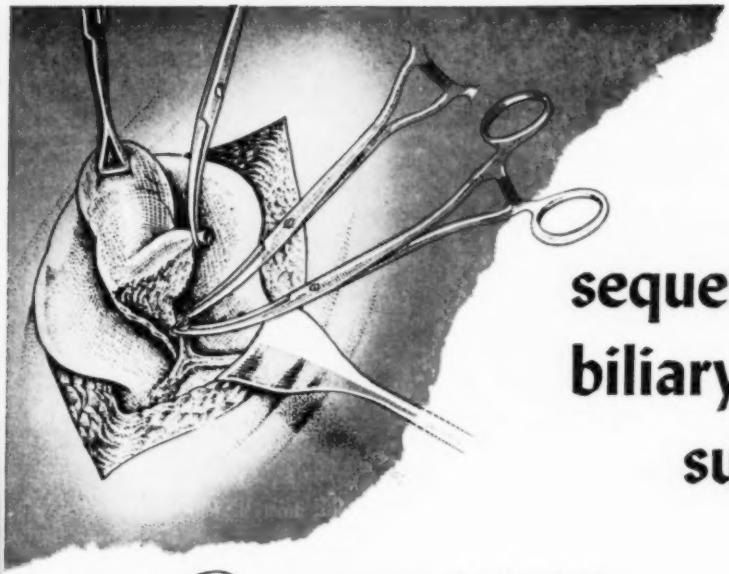
2. FACT Minor side effects, such as nausea, gastrointestinal upset, headache, etc., occur with Ertron as with many other valuable drugs. However, toxicity severe enough to warrant cessation of Ertron therapy occurred in only 1.4% of 1,020 arthritic patients. This incidence is low particularly when compared with the incidence of gold toxicity, which varies from 20% to 40%.

Conclusion Tolerance to Ertron is high. Treatment can be conducted without serious mishap if normal precautions are taken, i.e., administration of proper dosage and periodic observation of the patient. Side effects respond to temporary interruption of therapy or reduction of dosage, and usually do not recur when treatment is resumed.

ERTRON is supplied in bottles of 50, 100 and 500 capsules, and Ertron Parenteral in packages of six 1 cc. ampuls. Each capsule contains 5 milligrams of activation-products having antirachitic activity of fifty thousand U.S.P. units. Each ampul contains activation-products having antirachitic activity of five hundred thousand U.S.P. units, in sesame oil. Biologically standardized.

Whittier

LABORATORIES · DIVISION NUTRITION RESEARCH LABORATORIES
CHICAGO 30, ILLINOIS



sequence in biliary tract surgery

preoperatively-Decholin

brand of dehydrocholic acid stimulates an abundant flow of thin bile, helping to "clear the arena" for surgery by the removal of inspissated bile, mucus, small stones and other accumulations from the choledochus. This powerful hydrocholeretic action also produces functional distension of the gallbladder and ducts, aiding in identification and surgical procedure.

postoperatively-Decholin

provides an effective means of flushing out the biliary tract. Used together with antispasmodics such as atropine and nitroglycerin, *Decholin* helps to remove blood clots, residual debris and hidden, small calculi. This method, recently re-emphasized by Best,[1] is useful with or without T tube drainage. In reflex biliary stasis, *Decholin* serves to prompt an adequate secretion of bile.

For more rapid and intense hydrocholeresis, *Decholin Sodium*, brand of sodium dehydrocholate, is given intravenously, followed by a course of *Decholin* tablets.

Decholin

brand of dehydrocholic acid

Decholin (brand of dehydrocholic acid) Tablets of 3¼ grains, in bottles of 25, 100, 500 and 1000.

Decholin Sodium (brand of sodium dehydrocholate) 20% solution, in ampuls of 3 cc., 5 cc. and 10 cc., boxes of 3 and 20.

1. Best, R. R.: Ann. Surg. *128*: 348 (Sept.) 1948.

DECHOLIN and DECHOLIN SODIUM: Trademarks registered in U. S. and Canada.

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how to get rid of

undesirable tenants

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single dose disposable applicators

Safe, dainty, easy-to-use **westhiazole® vaginal** rapidly produces.

1. **a vaginal acidity untenable** to most pathogenic organisms.
2. **speedy control** of discharge, itching, foul odor, and other distress.
3. **more rapid recovery** by elimination of secondary as well as primary infection; recovery in vaginitis averages 2 to 7 weeks; in cervicitis 3 weeks.

westhiazole vaginal jelly contains 10% SULFATHIAZOLE, 4% UREA, 3% LACTIC ACID, 1% ACETIC ACID in a polyethylene base.

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like child's play

—giving accurate doses of vitamin C

When you specify Cecon, it's easy for anyone to give an infant the correct dose of vitamin C by simply measuring so many drops of Cecon into the formula or juice. For older children it's even easier—they can be given their vitamin C in candy-like Cecon *Dulcet** Tablets. • Cecon has 2.5 mg. ascorbic acid in each drop from the special Cecon dropper—that's 100 mg. per cc. The solution is stable for months without refrigeration, does not oxidize or settle out. No tablet crushing, no tablet chips left in nipple or cup. Supplied in 10-cc and 50-cc. bottles with dropper tops. • The delicious new Cecon *Dulcet* Tablet contains 50 mg. ascorbic acid. These sugar tablets come in bottles of 100. Youngsters like their vitamin C in this form—as do many adults. Your pharmacist has both Cecon and Cecon *Dulcet* Tablets.

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

CECON® ABBOTT'S ASCORBIC ACID IN LIQUID AND IN DULCET* TABLET FORM

*MEDICATED SUGAR TABLETS, ABBOTT T.M. REG. U.S. PAT. OFF.

Landmark in Cancer Research

Christopher Howard Andrewes, F.R.S.

London, England

Since the discovery, a century or so ago, that disease could be caused by bacteria and similar minute parasites, investigators have discussed the possibility that cancer might have a parasitic cause. Many claims to have discovered such a cause were made, but all were soon disproved; the microscope revealed nothing within the cancer which could reasonably be regarded as a causative organism. There still remained, however, the possibility that a virus, a sub-microscopic organism, was responsible. Most pathologists were against such an idea. Cancer was not infectious. Experimental cancer could be studied in, for example, mice, but could only be propagated from mouse to mouse by grafts of minced tissue; it could be clearly shown that this was possible under the conditions of these tests only when intact living cancer cells were transplanted; the evidence was against the infection of the normal cells of the mouse receiving the graft. So strong were the arguments for this view that it was almost universally accepted.

Then, just 40 years ago, Dr. Peyton Rous, of the Rockefeller Institute, described a malignant tumour in a Plymouth Rock hen. This was accepted as an ordinary malignant growth until the following year he succeeded in infecting other hens by means of dried tissue and of cell-free filtrates of the growth. In other words, this hen-cancer clearly had a continuing cause separable from the living cells. This was contrary to all accepted cancer doctrine; so pathologists escaped from their dilemma by denying that the growth in the fowl was cancer at all. Rous patiently accumulated facts which made it certain that this—and other filterable fowl-tumours discovered meanwhile—behaved so exactly like other cancers in all other essential respects that it was sheer nonsense to try to deny them the appellation of cancer. Meanwhile, a few other filterable cancers were discovered, a kidney- tumour affecting leopard frogs in Vermont, and a warty growth going on to cancer in cotton-tail rabbits from Kansas. This last has again been most fruitfully studied by Dr. Rous. Finally, Dr. Bittner, in Minnesota, discovered that breast-cancers in mice developed because those mice as sucklings had taken in with their mother's milk a filterable multiplying agent having all the properties of a virus. The doctrines of 40 years ago still have such a hold that most pathologists hesitate to speak of a virus in this connection and still refer to this breast-cancer virus as a "milk-factor" or an "influence"; it is now known, however, to have all the properties of viruses and its picture has been taken within cancer cells by the electron microscope.

Various Causes

Let us consider another side of the story. New cancers can be produced in mice by a variety of agents, by painting with tar, by x-rays, by ultra-violet irradiation, by injecting certain pure chemical substances. Every pathologist nowadays has to admit that some cancers may be due to viruses, but most of them say a virus is only one, and that a rare cause; chemical and unknown agents are much more usual causes; the virus cancers of hens, frogs and cottontails are zoological curiosities. Rous, in the United States, and Gye, in Britain, were quick to point out that the tumour-producing action of viruses showed an important difference from that of the

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other agents. The tar and x-rays were active in causing a cancer to start; once it had begun they played no further part in keeping it going. Tumour-viruses, on the other hand, multiplied within the growing cancer cells, constantly driving them on in their malignant course; they were a continuing cause. The few who held that viruses were important in all cancers felt that the difference between Rous' fowl tumours and other experimental cancers might be merely one of degree, that improvements in technical methods might show that there was no fundamental difference between the tumours of the two species.

Now, exciting news of such technical advances has come. Professor W. E. Gye, of the laboratories of the Imperial Cancer Research Fund, has reported in a lecture to Britain's Royal College of Surgeons that a number of mouse cancers can be transmitted by means of dried tissue. It is not easy to convey the significance of this apparently dull and certainly very technical finding. It is, however, a landmark in cancer research. It is not believed that mammalian cells can be thorously dried and yet survive. Therefore, what for long seemed not to happen has now been shown to happen: mouse cancers —and by implication cancers of other mammals including man—can be produced by injection of a multiplying continuing agent which can be separated from the cancer-cell itself. In other words, something infects cells—just like a parasitic microbe—causes them to be cancerous and is recovered in increased quantity from the new cancers. Almost certainly, that active agent, since it cannot be seen in ordinary microscopes, is a virus.

This is what Gye claims on behalf of his colleagues and himself. Can we accept it as fact? There have been earlier claims to have established a parasitic cause for cancer, and they have not stood up to critical tests. Are we any surer now? Gye's first evidence is that mouse cancer cells can be frozen for long periods and far below freezing point without losing the power to produce cancer. They can be safely treated with strong glycerine and strong sugar solutions which no whole cell would be expected to survive. In all these cases, however, there is room for argument that the cells were not all dead. But drying is a different matter, and Gye has employed drying to a very dry powder indeed. Gye himself and many others in past years have tried to dry mouse tumours again and again, and have failed. Two improvements in technique have brought success. First, Dr. Craigie has made a better drying machine. Secondly, it has been found that there are immense advantages in freezing the cancers for some time before drying them; the active agent is far more likely to survive, and, indeed, may not survive at all if the preliminary freezing is not carried out. One can speculate as to the reason why this preliminary freezing is so useful, but one lacks real evidence on the point. In the printed account of his lecture, Gye reported that three connective-tissue tumours or sarcomas had been successfully dried; in the lecture itself he gave stop-press news that the same had been achieved also for three breast-cancers, all of mice. If he had succeeded with one, or even two, mouse tumours, one could perhaps relegate them to the curiosity collection along with the growths of leopard frogs and cotton-tails. But here seems something more, a means of showing, by use of new techniques, a general principle which brings tumours in general into line with those which seemed to be only curiosities.

Necessary for Conviction

Three things are necessary for our complete conviction.

(i) It must be clearly shown that this drying can be produced at will with all sorts of tumours. We must be absolutely certain that we are not still wandering in the curiosity museum.

(ii) We must be absolutely sure that no living cells in these cancers have survived the drying. It is hard to prove a negative, but we must have that degree of certainty which would enable a jury to convict. All we know of complex mammalian cells suggests that they would disintegrate into

—Continued on page 521

SPECIAL ARTICLE

Rabies

This summarization attempts to cover the essential therapeutic information on the subject and is designed as a time-saving refresher for the busy practitioner.

Reprints available*

Definition

Rabies is an acute infectious disease usually found in lower animals. It is caused by a neurotropic filtrable virus which is found in the saliva, salivary glands and certain nerve tissues. Transmission usually is by the saliva through biting, and occasionally by contact between an open wound and infected saliva or tissue and experimentally by inoculation with infected tissues. After a varying incubation period the condition which results is characterized by pathological changes in the motor nerve cells of the basal nuclei and cord, psychic excitation, paralysis and then death.[1, 2] Although rabies does not provide a major problem in public health in the United States because of the strict controls over stray dogs and cats, the fact that once it has developed in a human being it is always fatal makes it very important that the general practitioner have a good practical knowledge of it. There are only a few instances which appear to be authentic[3] in which recovery has been reported.

Historical Background

Aristotle, Celsus and Galen all described rabies so that it is not, by any means, a new condition. The fact that it is infectious in nature was first demonstrated by Zinke in 1804 when he inoculated healthy animals with saliva from rabid dogs.

Pasteur devoted considerable time and effort to the study of rabies and in 1881 he was able to prove that the virus is found in the central nervous system and subdural inoculation with the brain from a rabid animal will transmit the virus. Three years later he reported on a method of protecting animals by injecting subcutaneously spinal cord containing the virus, which virus was modified by passing it through a series of rabbits and finally dried for attenuation.[1]

Incidence

Contrary to popular belief rabies is not a seasonal disease nor is it related in any way to the time of year described as "dog days." It may occur in any country, in any climate and at any time of the year. England has been free of rabies since 1923 and since 1903 there have been no human deaths. In the United States, however, there have been 3000 deaths from rabies during that time. Its incidence appears to be greatest in California, Texas, Georgia, Illinois, Ohio, Tennessee, Pennsylvania and Louisiana. No cases of rabies have ever been reported in Australia and New Zealand and it is relatively rare in the Scandinavian countries, in Holland, Germany and Switzerland. In Belgium, France, Italy, Russia, China, India, Indo-China, Japan and the Dutch East Indies it is relatively common.

Rabies is found in every part of the United States and in some areas it appears to be increasing. According to statistics there have been 42,510 cases (animal and human) of rabies in the United States in

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the period from 1940 to 1944. In a 10 year period from 1930 to 1940 the number of human cases averaged 55 annually.[3a 3b] Periodically there are reports of outbreaks in certain areas, as for example in California in 1937 there were 2000 rabid animals and 3 human cases. In Illinois in 1936 10 humans died of rabies. In Pennsylvania in 1938 there were 493 rabid animals of which 365 were found in 4 adjoining counties. In more recent years Texas and California have shown the greatest incidence of rabid animals and Texas and Tennessee of human rabies cases.[2]

Sources

The dog is chiefly responsible for rabies but it is prevalent also in other members of the canine family such as wolves, foxes, coyotes, hyenas, and jackals. Because these animals have sharp teeth which are their chief weapon for offense and defense it is easy for them to transmit the virus because they bite more deeply. Also the virus is increased in its infectivity after passing through carnivora such as these. All members of the mammalian family and most warm-blooded animals are susceptible to rabies and therefore develop it after being bitten by a rabid animal. The reserve of infection is easily maintained by as few as four infected dogs a year because the incubation period of the virus in dogs is so long (90 days or more).

A study of human rabies has shown that possibly 10 per cent of the cases may be feline in origin whereas the other 90 per cent are all of canine origin. In most instances, however, the feline rabies was canine in origin. There have been infrequent reports of rabies when a human was bitten by a horse, mule, cow, skunk, squirrel, sheep, pig or some other animal which had previously been bitten by a rabid dog. It has never been demonstrated that rabies can be transmitted from one human to another.

There are certain blood-sucking bats native to Central and South America which also are capable of transmitting rabies. The large bats or flying foxes of the South Pacific and rats do not appear to be capable of its transmission. In the case of rats it is believed that the infection is so virulent that the incubation period is shortened and the disease is eliminated along with the infected animal so that a reservoir cannot be built up in any one colony.

The most common reservoirs of the infection are the canine of which there are 2 types, the domestic or the dog and the wild which includes the wolves, foxes and the like. Wolves have played an important role in continuing rabies in Russia. Coyotes have caused outbreaks, particularly in cattle in North America. However, the dog still remains the most important reservoir of infection.[2]

Etiology

The virus which causes rabies is filtrable. Certain chemicals as well as heat, drying and sunlight will alter or destroy it. After the virus has entered the body it travels through the nerves to the brain where it multiplies, passes on to the salivary glands along the efferent nerves and then into the saliva.

Probability of Infection

Of those humans bitten by a rabid dog or other animal approximately 16 per cent will become infected. Some believe that the chance of contracting rabies from a bite of a proved rabid dog is approximately 5 to 15 per cent.[4] However, there are several factors which vary with the individual and which influence the probability of infection: the number of bites; the type of wound (badly lacerated or deep puncture wounds are more serious); whether the bitten area was clothed or not (the tooth is partially cleansed by clothing before penetration); and the type of animal (the wolf is worst with the cat second, the dog third and other animals last).

From data assembled in Europe Table I shows the chances of infection under various conditions.[5]

Rabies in humans is generally found among those persons who come in contact most frequently with animals either because of occupation such as farmers, veterinarians, dog breeders or because they own them for pets. Before rabies is

TABLE I.

TYPE AND LOCATION OF WOUND	ANIMAL CAUSING WOUND	CHANCES OF INFECTION, PER CENT
Multiple, deep: eye, nose, lips	Wolf	100 per cent
Multiple, deep: eye, nose, lips	Cat	70 per cent
Multiple, deep: eye, nose, lips	Dog	60 per cent
Multiple, deep: rest of face	Dog	50 per cent
Multiple, deep: rest of bare areas	Dog	30 per cent
Single, deep: fingers, neck	Dog	15 per cent
Superficial: uncovered areas	Dog	10 per cent
(but if these bleed freely)		2 per cent
Infected saliva on a recent wound		0.1 per cent
Infected saliva on a 24-hour-old wound		0 per cent

suspected in the animal a human may contract it in the process of examining the animal for some other disorder. It is especially difficult to treat a bite through the thumb nail. Laboratory workers who must dissect the head of a rabid animal may develop the infection. If a person with a fresh wound comes in contact with furniture or rugs or the like which may have infected saliva on them it is possible to contract the infection but it is not likely because drying alters and destroys the virus.

Pathology

The virus enters the body, usually through a bite, and is deposited by the saliva deep in the wound. In some instances it may enter by way of a scratch or minor abrasion. From here the virus is thought to invade traumatized nerves along which it passes centrally to the cord or brain. Because the data on this theory are not too substantial as yet, the possibility that the virus also may be transported by the blood or lymph is being investigated.

When an autopsy is performed various changes are observed. The vessels in the meninges and brain usually show congestion. The nerve cells show degenerative changes ranging from chromatolysis to neuronophagia and are surrounded by inflammatory and phagocytic cells. In the brain there are diffuse and perivascular infiltrations of small round cells. The gasserian and sympathetic ganglia are usually infiltrated with endothelial cells and the nerve cells are destroyed. Some of these changes also may be observed in other conditions so that diagnosis generally is based upon the finding of eosinophilic Negri bodies in the cytoplasm of the ganglionic nerve cells and particularly in the hippocampus. In some few cases it may be impossible to find these bodies. If such is the case possible diagnosis as rabies should not be dismissed entirely. The most characteristic changes are observed in the spinal cord and particularly in the segments which control the area bitten and in the spinal ganglia and midbrain.[4, 5]

Diagnosis

Diagnosis of rabies is based upon the history of exposure, clinical symptoms and course, the termination, the microscopic demonstration of Negri bodies and animal inoculation.[6] The first three factors are of considerable importance if the laboratory diagnosis is negative but generally they are chiefly presumptive. There may be no history of exposure available, the clinical symptoms may be atypical, and recovery is not always conclusive that the condition was not rabies.

Microscopic diagnosis of rabies is based upon the observation of the Negri bodies in the nerve cells of the suspected animal or in those of other animals which have been inoculated with brain material from the former. The Negri bodies are characteristic[7, 8] but no explanation has been developed for their presence or of what they consist. It is possible that they may be inclusions, virus colonies, protozoa or by-products of cellular degeneration. As stated previously, however, failure to find these bodies in various specimens does

not necessarily preclude rabies.[6] In diagnosis of rabies in animals it may be preferable to send the entire head to the laboratory. It cannot be sent by U. S. mail and Railway Express has given specific rules to its agents for this: [9, 10]

TABLE II

Rules and regulations governing the shipment of the heads of dogs or other animals by express to laboratories of state boards of health or other laboratories.

a. Agents must not accept for transportation the head of a dog, or any other animal, sent to state boards of health for rabies examination, unless it shall have been prepared for shipment as hereinafter provided.

b. The head of a dog or other animal so shipped must be placed in a tin can or other metal container, which will not permit the leakage of fluids; such container shall then be placed in a second metal container with ice packed around it; such outside container must be so constructed that it will not permit the leakage of the ice water.

c. All such packages must be labeled: Caution—This package contains the head of a dog (or name of other animal) suspected of having died of hydrophobia.

d. Such shipments tendered on Saturday, which cannot reach destination early enough for delivery on that day, and would, therefore, remain in the express office over Sunday, must be refused, and shipper requested to pack in ice and hold until Monday, so that they can be delivered without delay at destination.

e. Require prepayment of charges on shipments of this kind.

Many state health departments have issued in pamphlet form complete instructions for collecting and transporting such material. Laboratory workers must use extreme caution in handling this material.

It is advisable to keep the suspected animal alive until symptoms develop.

Positive diagnosis is generally based upon animal inoculation. This is done by inoculating intracranially into rabbits, guinea pigs or mice some of the brain material from the suspected animal. This method is of value in the final diagnosis but because of the long period (10 to 20 or 30 days in rabbits or guinea pigs) is of little value in public health procedures. A period of such length cannot be allowed in making a decision as to whether the exposed humans should be treated with preventive measures. However, a mouse inoculation test now devised may be of some use since Negri bodies appear in some in 5 to 6 days and death usually occurs in 10 to 12 days.[6-8, 11-13]

Diagnosis of human rabies is of course based upon the findings in the suspected animal, the symptoms of the patient and the general background of the case. If death occurs it is important that a final diagnosis be made in order to protect other humans. The hippocampus should be dissected and smears made from the cut surface. Giemsa, Mann or other staining methods for inclusions should be used. In addition to the smears sections should be made from the hippocampus and other portions of the central nervous system which are fixed and stained and studied for presence of Negri bodies. Portions of the medulla, cord and other parts of the central nervous system should be ground. The resulting suspension should be inoculated intracerebrally in mice or rabbits.[4, 6, 11-14]

Incubation

The incubation period for rabies varies with the strain of the virus, the species of animal, the human being, the extent of the bite and with the distance from the bitten area to the central nervous system. In dogs the incubation period is shorter than in humans and in children it is shorter than in adults. If the bite is on the face or head the incubation period is shortest whereas if it is on the foot the incubation period is longest. This is based upon the fact that the virus passes along the peripheral nerves to the brain and the shorter the distance the less time it takes for symptoms to develop. In humans the incubation period may vary from 10 days to 2 or more years with the average between 50 to 60 days according to some.[1] Others state that symptoms may develop in 12 days after a face bite and in as long as 11 months after a foot bite. However, the average incubation period is usually 20 to 90 days.[2] It is said that in dogs the period varies between 15 and 30 days on the average but may be a year or more,[1] whereas others claim that the average is between 20 and 40 days with extremes between 12 and 113 days.[2, 15]

The dog begins to be infective (virus

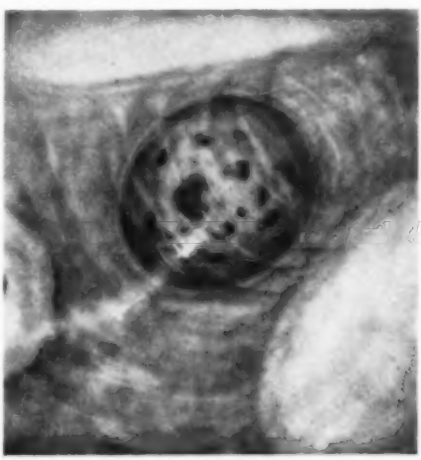
appears in increasing quantities in the saliva) during the last 5 to 8 days of the incubation period. The virus continues to increase until death occurs. It has been reported that the virus has appeared in the dog's saliva as early as 12 days after infection.[16] Because of this possibility the dog may appear in good health but his saliva already may contain the virus. If the bite was inflicted 14 days before symptoms develop in the dog the human who was bitten probably is safe from the rabies.[2]

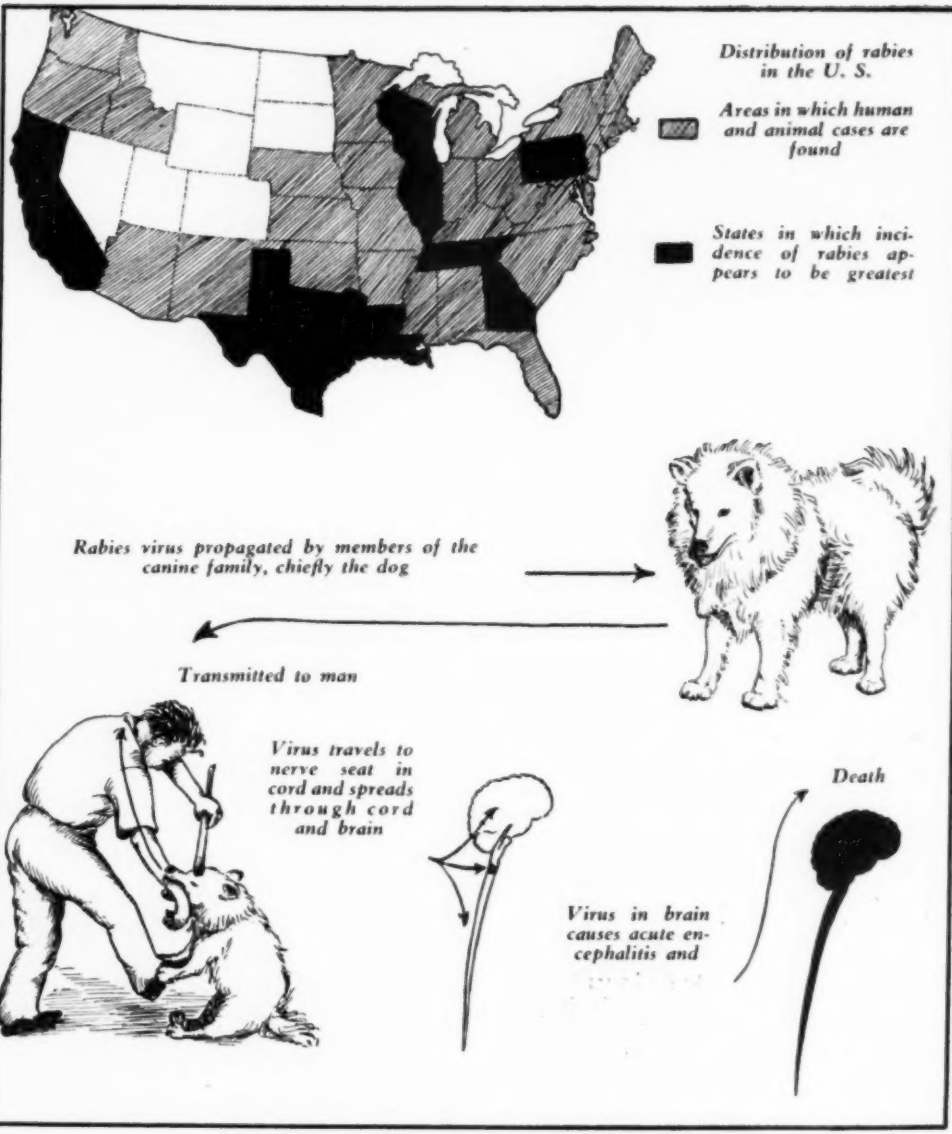
Symptoms

There are three stages of rabies in man—the prodromal, the excitement and the paralytic stages. The first stage lasts for approximately 48 hours and is characterized by mental depression, insomnia, a sense of impending danger, irritability, uncontrollable restlessness, anorexia and melancholia. There may be tingling sensations and soreness, particularly in the bitten area. As the irritation to the central nervous system increases the excitement stage sets in somewhat abruptly.[17]

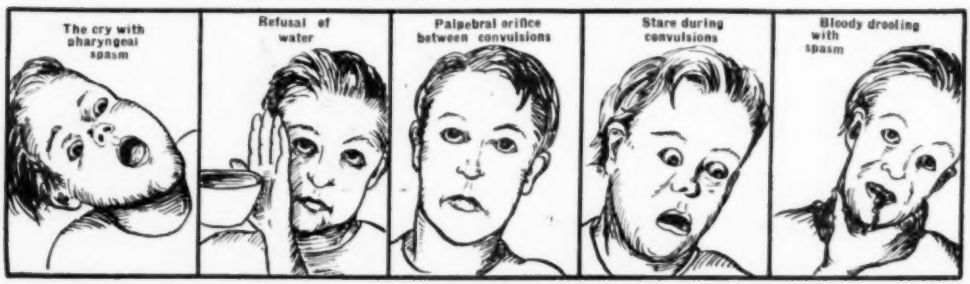
This stage is characterized by choreiform tremors, hyperesthesia of the sense organs and general excitement. In this respect the skin becomes very sensitive to changes in temperature, particularly to currents of air, and there is also an increased sensitivity to sound and light. The restlessness becomes an ungovernable agitation and the terrified patient may become maniacal. Spasms are severe and become apparent first in 24 to 48 hours in the throat muscles and larynx. This is generally brought on by attempts to swallow and consequently swallowing is impossible. This causes the patient to be unwilling to even try to swallow food or water. The common name for rabies is hydrophobia or a fear of water but this is simply a reaction to the unsuccessful attempts to swallow.[2] This laryngeal spasm is most always observed and it is caused by the reflex irritability of the deglutition center. The condition is very agonizing to the patient and distressing to the attendents and is probably the basic cause for the fear of this disease. After the patient has made several attempts the pain becomes severe and although his thirst is unbearable he cannot be forced to swallow and simple raising of the glass of water to the lips or sight or mention of water causes the muscles of deglutition to contract like a vise and the glottis and pharynx become unbearably painful. Convulsive movements pass through the body, the jaws are clenched and respiration is stopped. A feeling of strangling is experienced and the patient may die during such a spasm. The patient usually finds it difficult to breathe in the very beginning and generally gasps for breath. The convulsions or muscular spasms gradually involve the entire body, and the least stimulus (slight irritation or current of air such as that caused by blowing the breath on the neck) will start an attack of convulsions. Each attack is followed by a few minutes of calmness during which the patient may show concern over those attending him and also may warn them of another attack. During these crises the mouth is filled with frothy, thick, tenacious saliva and because of the inability to swallow it pours out of the mouth. Respiratory difficulties are precipitated by the slightest breeze and result in spasmodic breathing and extreme dyspnea. There is an increase

Negri body in nerve cell





CHARACTERISTIC SYMPTOMS OF RABIES



in the reflexes and at first the pupils are contracted but later they become dilated and fixed. The patient frequently may have visual and auditory hallucinations and may show other signs of mental derangement. As the attacks progress the patient becomes uncooperative and maniacal.

The third stage is that of paralysis which follows rapidly after the excitement stage. Frequently it is first observed in the muscles in the area of the bite and may remain local or may become general and involve the tongue, face and eyes. It is usually a flaccid paralysis. A rising fever and pulse rate are accompanied by moderate leukocytosis. The patient becomes quiet and more and more feeble with a lessening of spasms and of respiratory difficulties. Once again he is able to swallow. The pupils become dilated and reflexes disappear. Death usually occurs gradually or suddenly as a result of cardiac or respiratory failure. The disease usually does not last more than 48 hours after the prodromal stage and the total time involved is 1 to 8 days.[1, 3, 4, 17, 19]

Some have stated that the paralytic form occurs in patients who do not experience cerebral irritation and that it is preceded by a high fever and neuralgic pains in the area of the bite. Weakness and paralysis of the muscles in this area precede a general paralysis which is followed by death.[1] However, others have stated that the substitution of paralysis for hydrophobia is rare[4]

There are two types of rabies in dogs and either may occur alone, merged with the other, or both may appear at different times. These are known as the "furious" type, which is similar to the excitement stage, and the "dumb" type, which is similar to the paralytic stage.

The furious type or excitement stage does not always occur in dogs and also it is more variable when it does occur. Usually the dog changes its behavior and temperament. The usually gentle dog may become morose, hides, refuses food and does not bark in the usual manner. In some instances the dog may become overly friendly and refuse to leave the side of its master or fawn excessively upon him and other household members. Within 12 to 48 hours it develops a restlessness which makes it come and go continually, resting in a reclining position for a short time and then abruptly jumping up and moving to another area with obvious agitation. The dog may not be able to remain quiet and acts as though something unnatural is compelling it to follow this procedure. It may obey any command and make no movement toward biting. Its agitation is increased after it has rested for a short period. Restraint of any kind such as keeping it in the house results in irritation and strangers may be attacked without any warning symptoms. Agitation and excitement result and the bedding may be scratched, torn and upturned and furniture attacked and gnawed. Any object pointed at it may be seized in a vicious manner. Home-loving dogs, if free, usually become restless and wander aimlessly at great distances from home, biting any dog they meet The dog generally does not go out of its way to fight other dogs, nor does it remain in the vicinity after it has bitten another dog. A previously affectionate dog develops a bad temper and aggressiveness and may bite its master.

Although the dog refuses its usual food it develops strange appetities and desires and may be found chewing on rugs, wood, stone and the like. As in humans the throat muscles develop convulsive spasms which make it difficult to swallow solid or liquid foods.

As the condition continues the dog begins to growl, bark hoarsely and snap at imaginary objects or anything in its path. It may even turn suddenly as though defending itself against something. Other domestic animals with which it has previously lived in peace may be chased. Eventually the entire body is involved in convulsive spasms and as paralysis sets in the haggard, emaciated dog which has wandered from home may fall in its tracks or may return home to die. Once the paralytic stage begins the dog soon dies. In some cases this may be the only stage and the preliminary characteristics may go unrecognized. There may be no excitement stage or it may be so slight as to be un-

observed. The dog becomes quiet, secretive and frequently more affectionate. The course of this stage is more rapid and evidence of illness is clear but the dog is only anxious, not excitable. Paralysis is first noticed, usually in the muscles of the lower jaw because the dog cannot close its jaw, the tongue protrudes and it drools saliva. In the first stages of paralysis of the jaw muscles it may be thought that the dog has a bone in its throat. Attempts at removal result in the hands becoming covered with saliva and possible infection if there is an open wound. The spread of paralysis to other portions of the body is rapid and generally the hind quarters are next affected so that the dog cannot move. Death occurs in 2 or 3 to 5 or 6 days (sometimes slightly longer) after the symptoms begin.[1, 2, 17]

Differential Diagnosis

Rabies or hydrophobia must be differentiated from tetanus, botulism and hysteria. A bite is very rarely the cause of tetanus and constant trismus is usually the first symptom of this condition. A characteristic involvement of the eye muscles (diplopia) distinguishes botulism. Fear of rabies by the patient may result in hysteria in which the symptoms closely resemble those of the real condition. However, this condition usually occurs shortly after the patient has been bitten and long before even the shortest incubation period could have passed. The precipitation of convulsions by blowing the breath on the neck is useful in differentiating rabies from hysteria. Assurance to the patient that he has not been exposed usually is helpful.[1, 2]

Prognosis

Rabies is always fatal once the symptoms have appeared. Bites on the face and head cause fatalities in 60 to 70 per cent of cases; on the hands, 15 to 20 per cent; and through clothing, 1 per cent. The mortality varies directly with the extent of the injury. Extreme heat or cold, fatigue, fear and alcoholism all play roles in the development of rabies.

Therapy

If the patient once develops rabies the only therapy indicated is palliative. The patient should be kept as quiet as possible in a darkened room. For sedation to control the pain and excitement large doses of sedatives, such as chloral, the barbiturates or morphine, may be given. It has been reported that one patient given the following medicaments within 24 hours still had to be shackled to bed: 0.75 Gm. pentobarbital sodium rectally; 0.6 Gm. phenobarbital sodium intramuscularly; 4 Gm. chloral hydrate rectally; and 60 mg. of morphine sulfate intramuscularly. Relief may be obtained and the ability to take liquid nourishment may be restored by spraying well down into the larynx with 5 per cent cocaine solution.[1, 21, 22]

A. Local

There are various types of local therapy recommended for treating the wound. If the dog is known to be rabid the wound first should be opened freely, making all parts accessible. Bleeding should be encouraged. Mechanical cleansing and cauterization then follow. For many years fuming nitric acid was used for this purpose in every case in which the biting animal was shown to be rabid.[23, 24] Such cauterization can be done in a relatively short time and is effective for 24 hours or more whereas with the Pasteur treatment or other antirabic vaccine therapy the incubation period may be too short. This may particularly apply in cases of face bites although there may be some objection, particularly in females, because of the possibility of scarring. A circle of petrolatum should be applied on the sound skin surrounding the area and the acid applied drop by drop by means of a capillary pipette. It should be placed on every part of the wound but not on sound skin.[25] This should be done even if 3 or 4 days have elapsed.[23]

In recent years there has been some controversy concerning the use of nitric acid. Some believe that it is more painful and no more effective than pure phenol followed by 95 per cent alcohol. Cauterization may not destroy all of the virus

but it will prolong the incubation period, allowing a greater time for preventive therapy.[1]

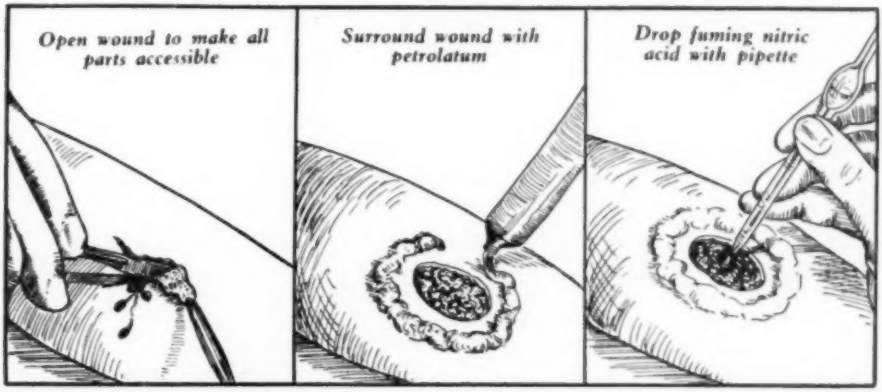
Because some believe any substance introduced into a wound is quickly carried away by the lymphatics they recommend that washing with mercury bichloride 1:1000 solution may be just as effective.[26] If it is possible to wash the wound within the first few hours some believe that irrigation with a 20 per cent solution of medicinal soft soap is just as effective.[27]

A suggestion that cleansing with soap and water and irrigation with saline solution some years ago[28] sparked the controversy and several excellent points were brought out in the ensuing exchanges of opinions: (1) The lymphatics or the blood stream are not the portal of entry for the rabies virus; (2) the rabies virus travels at a very slow rate along the nerve trunks to the brain; (3) fuming nitric acid has in addition to its destructive properties on tissue and virus a penetrating effect which allows it to destroy the virus at a greater depth; (4) as much virus as possible should be destroyed at the portal of entry because the vaccines available can only protect the patient against a limited quantity of virus; and (5) scarring of the face should not be used as a contraindication for cauterization because it is more urgent that it be done here due to the close proximity to the central nervous system.[29]

B. Vaccine Treatment

Many years ago Pasteur discovered that if the virus from a rabid dog known as "street" virus is passed through a number of rabbits its virulence for rabbits is increased and it becomes known as "fixed" virus because its incubation period is shortened gradually until it is fixed between 6—7 days. This fixed virus is much less virulent for man than the street virus is and it can be attenuated by drying, under sterile conditions and precautions in a flask with caustic potash, the spinal cord of a rabbit which died from the infection. In 24 hours the cord still possesses approximately as much activity as the fresh material; in 48 hours there is much less activity and in 8 days there is no activity. However, the cord still retains some of its antigenic powers. If further destruction of the virus is desired treatment in glycerin will accomplish this. Active immunity against the "street" virus can be produced in animals and humans by injecting each day an emulsion of the rabbit cord dried for 14 days. Each day after this cords dried one day less are used. The usual course of injections is about 14 but 21 may be advisable in cases of severe multiple bites and particularly if the head is involved.[2] Figures gathered by one worker showed that the mortality was 0.23 per cent in 69,541 patients given this therapy[30] Additional statistics have shown that failures when using the prophylactic

Local Measures in Treatment of Wound



vaccine resulted in 0.26 per cent in cases with arm bites and 1.59 per cent in cases with head bites.[31] As stated earlier the mortality rate without therapy is approximately 16 per cent. Although some have questioned the efficacy of the Pasteur vaccine treatment[17] others believe that at present there is no justification for not using it.[1, 21, 32]

Heat and dilution also have been used as methods of reducing the potency of the virus. Semple introduced a phenol-killed virus vaccine which rapidly became more popular than the attenuated vaccine of Pasteur. Along with a chloroform-killed virus vaccine it was believed to be just as effective as Pasteur's and much less likely to cause postvaccinial effects.

Because the commercially prepared vaccines varied in potency a test for standardization was devised and is now employed.[33, 34]

Although various modifications are available the most common product is a 4 to 5 per cent suspension of infected nervous tissue with 0.5 per cent phenol. Although there are no amounts of live virus detectable there will be considerable foreign nerve tissue injected in the dosage of as much as 10 cc. daily for 7—14 days.[4] It is administered subcutaneously following sterile precautions and a different quadrant of the abdomen is used each day. The site selected should be as far as possible from the site of the previous injection. Some believe that injection into the buttocks is less painful.[21] The usual dosage is 2 cc. for persons of all ages but in cases where the wounds are multiple, deep, lacerating or involve the head or neck it may be necessary to give larger quantities of vaccine. This is known as the "intensive treatment."

Because the commercially available products are made up in vials containing one dosage it is generally considered that the dosage is the content of 1 vial, which is given for 14 or 21 days. Where intensive therapy is desired the contents of 2 vials may be given daily for 7 days followed by 2 doses daily for the second week. The suspension is made in physiologic saline from finely ground brain and spinal cord tissue of rabbits killed approximately 6 days after inoculation with the fixed vaccine. The virus may be phenol-treated to kill it; it may be attenuated by freezing with carbon dioxide snow followed by rapid vacuum drying (Harris method); or it may be inactivated with ultraviolet light. The single dosage vials vary from 0.5 cc. to 1 cc. to 2 cc. and are packaged in units of 7 or 14 or both. Some are also packaged with a syringe and needle. Virus grown in tissue culture has also been used in the live or inactivated state. Such a virus grown thus also may be killed by ultraviolet light as is the animal brain suspension. The virus also may be rendered inactive with formaldehyde, chloroform or ether. Some believe that the irradiated vaccine is superior because it can be stored more easily, does not lose its potency and seemingly induces a higher degree of immunity. However, the phenolized vaccine is easily produced and maintained in a sterile condition, is readily transported and easily administered. The desiccated cord vaccine and diluted vaccine (Hoyges) are considered to have certain disadvantages because they contain the live virus.[3b]

Vaccination with these vaccines is indicated immediately in the following conditions:

1. If the dog is undoubtedly rabid.
2. If the person is bitten through the skin and the animal escapes or if it is caught and rabies cannot be proven or the dog cannot be proven nonrabid.
3. If the dog was shot immediately it is possible it may have been in the incubative stage with virus in the saliva but no Negri bodies in the brain.
4. If the bites are located on the face or neck the incubation period is too short to ascertain whether rabies develops in the dog within 2 weeks. If the dog is still well in 14 days therapy may be stopped.
5. If the head, when it reaches the laboratory, is too decayed.
6. If a wound less than 24 hours old is contaminated with saliva.
7. If a known rabid dog has licked a young child's or infant's face.
8. If the dog is caught and is kept under

observation in a veterinary hospital for 14 days and he dies in that period the head should be sent to the state laboratory for diagnosis. If there is a positive laboratory report or the veterinarian is able to diagnose the condition as rabies preventive therapy should be begun.[2] Some recommend vaccine therapy in all persons not bitten but who came into intimate contact with the rabid dog and were moistened by saliva.[2, 17] Others believe that mere licking by a rabid dog is not sufficient to indicate therapy and advise that it be given only to those infected with a potentially lethal dose of the virus or "at risk."[4]

The mechanism whereby antirabic vaccine works is not well understood. It is possible that the vaccine stimulates antibodies and nerve resistance which hinder the progress of the virus along the nerve fibers. Another theory is that there is an interference phenomenon in that the street and fixed viruses meet and cancel each other in the central nervous system.[4]

In those cases in which the vaccine failed to protect the individual death resulted for one of 3 reasons: (1) the vaccine had no effect; (2) administration of foreign nerve tissue may cause a nervous illness with resultant death; and (3) presence of fixed virus in vaccines containing live virus may cause death.[4]

Duration of immunity with these vaccines may last from 12 to 14 months at the most so that a suspected bite within a year of previous therapy should be again treated with a full course of injections. Reports have been made of 4 such treatments in 4 years, 3 in 4 years and 2 in 17 years.[35] Another worker found that 3 individuals required an additional course in 6 months. Skin tests with diluted vaccine (1:200) were negative so the injections were given. Because one person suffered side reactions believed to be psychic in origin the vaccine was given as a trial dose of 0.1 cc. and the entire dosage given after 2 minutes. No untoward reactions were observed.[36]

Although the vaccines render an active immunity they do not cure and therefore they should be administered as soon as possible before the disease can gain a foothold.[37]

Reactions

There are certain reactions which may follow injection of fairly large quantities of animal nerve tissue. Such reactions include neuroparalytic accident, polyneuritis, erythematous or urticarial rashes, *rage de laboratoire* and occasionally syncope. Neuroparalytic accident is used to describe an illness not attributed to invasion of nerve tissues by either type of virus but the symptoms resemble landriform paralysis or paraplegia caused by myelitis. There may be paralysis of certain local areas such as of the limbs, eye muscles, face and pharynx. Generally such a condition develops in 2 weeks after beginning of therapy. They are believed to be more common with those vaccines containing activated virus since it has been reported that 1 in 8887 persons developed this sequela when treated with phenol-inactivated virus. in a study of 1,060,832 treatments with active or inactivated virus the incidence was 181 (48 fatalities) or 1 for each 5861 and 1 fatality for each 22,100.[21] Others report an incidence of 1:3500 persons treated with desiccated cords and 1:8500 treated with phenolized vaccines. It is thought that the condition may be due to an immunity which develops in a sensitive person to a constituent of the normal rabbit or other foreign animal tissue in the vaccine rather than to infection by the vaccine.[1, 4]

With the Pasteur treatment another worker has reported such a condition in only 6 of 37,500 patients. The mortality was 16 per cent and the others recovered completely so that therapy even though myelitis develops should not be contraindicated.[38]

Rage de laboratoire is reported rarely but it may be more common than is thought. Ascending paralysis without hydrophobia occurs and after death the fixed virus can be isolated from the brain. A live vaccine is believed responsible.[4]

The polyneuritis is generally accompanied by facial paralysis.[22]

No ill effects on pregnant women have been reported.[24]

In some sensitive patients intensive therapy may cause some of these reactions. Because of the seriousness of some of these

reactions it is believed that the vaccine should not be given if the animal appears nonrabid and acts normally under observation.

It is believed that these reactions are allergic in nature and there have been published several reports in support of this. It was first suggested in 1907 and since that time others have substantiated it.[38a-38c] Consequently, it has been recommended that the patient should be tested for personal and familial allergy. By means of skin tests this can be determined and if positive the patient can be desensitized by the following schedule:

First day—0.5 cc. of a 1:100 dilution of vaccine

Second day—1.0 cc. of a 1:100 dilution of vaccine

Third day—0.5 cc. of a 1:10 dilution of vaccine

Fourth day—1.0 cc. of a 1:10 dilution of vaccine.

Fifth day—0.5 cc. of undiluted vaccine

Sixth day—1.0 cc. of undiluted vaccine

This schedule is based upon those vaccines made up of a 5 per cent emulsion of brain tissue. If a different concentration is employed it should be adjusted accordingly. If a patient shows a sensitivity to the vaccine in the skin tests or if he develops a local or systemic reaction he should be given the vaccine only if there is great risk of rabies. It should be given as outlined in the above schedule for the usual course of treatment.[38a-38e]

Some recommend that each case be managed individually. It has been reported that the antihistaminic agents, diphenhydramine hydrochloride and tripelennamine hydrochloride have produced complete recovery in one patient with encephalomyelitis and in one with dorsolumbar myelitis caused by the vaccines. The antihistaminics therefore appear to have a logical place in this therapy and it is probable that some of the others also would be effective.[38f]

Recently a new vaccine, which is believed to have fewer toxic effects, was reported. It is hoped that this vaccine will eliminate some of the difficulties now encountered.

C. Immune Serum

Antiserum (immune serum) alone or in conjunction with the vaccine has given encouraging results experimentally and is being tested further.[4] Although it has failed in humans thus far it is believed to have a definite place in prophylaxis and warrants additional clinical trial.[38g]

Treatment if Nonrabid

If the animal shows no signs of rabies the wound should be cleansed with soap and water, debrided if necessary and closed if indicated. Further treatment is not necessary if the dog shows no signs of rabies in 14 days.[23]

Treatment of the Dog

If the dog is obviously rabid it should be killed and its head sent to a laboratory for diagnosis. However, if the dog can be caught without harm to others and can be kept under observation so that a definite diagnosis can be made, it is preferable. If the dog is killed early in the disease Negri bodies may not be present in the brain since the saliva may contain the virus 4 to 6 days before the symptoms appear. However, if the dog remains normal for 10 to 14 days it is not rabid and has not passed on any infection. It is preferable to keep an animal, suspected of rabies, alive if possible, since even a light case of rabies will eventually be observed and all animals having any kind of case die without fail.

Animals bitten by other rabid animals should be destroyed if possible. However, in many cases quarantine of 3 to 6 months may be all that is necessary.[39] It has been reported that one dog developed rabies in 113 days after being bitten by a rabid dog.[40] If the animal has rabies or during quarantine shows signs of it or develops it, it should be given 14—21 doses of antirabic vaccine.[39] However, the incubation period is so short that effective therapy is almost impossible.

Immunization of dogs is possible before they are bitten but thus far it is both expensive and not always too effective.[2, 37] Some have reported value using one subcutaneous injection of 5 cc. of a chloroform-treated vaccine. It is believed that Negri bodies do not develop in dogs given preventive therapy.[41] Some feel that a sec-

ond dose may be necessary.[42] However, in New York City only one injection is required.[43] In Brazil cattle given one injection each year for 3 years are reported to be immune from vampire bats.[44]

Control

To control and finally eradicate rabies a properly planned and enforced program in which everyone cooperates is necessary. With nationwide cooperation national control may not be necessary.[24, 45-47] Unfortunately, the present local programs are generally neglected until there is an outbreak and as soon as it is over the program is forgotten.

A proper program enforced uniformly and nationwide would include the following measures:

1. Enforced licensing of all dogs.
2. Elimination of stray dogs (not necessarily ownerless).
3. Muzzling of dogs (not alone but in conjunction with the other measures).
4. Quarantine on canine immigration.
5. Immunization of dogs (a course of at least 5 doses of good vaccine and repeated once or twice at annual intervals).
6. Intelligent and active cooperation of the public.[2]

Bibliography

1. Harris, D. L. in A Textbook of Medicine 7th ed., ed. by R. L. Cecil, W. B. Saunders Co., Phila., Pa. 1947.
2. Kern, R. A.: *Med. Clin. of N. America* 1406 (Nov. 1944).
3. Hurst, E. W. and Pawan, J. L.: *Lancet 11*:622 (1931).
3a. Johnson, N. N., *et al.*: Report of the Subcommittee on Rabies. National Research Council, 1945.
3b. Pickar, D. N.: *Ky. Med. J. 47*:320 (1949).
4. Rhodes, A. J. and Van Rooyen, C. E.: Textbook of Virology. Thomas Nelson and Sons, New York, N. Y. 1949.
5. Babes, V.: Traite de la rage. J. B. Balliere, Paris, 1912.
6. Sellers, T. F. and Carnes, H. in Diagnostic Procedures and Reagents, 1st ed. American Public Health Assoc., New York, N. Y. 1941.
7. Leach, C. N.: *Am. J. Pub. Health 28*:162 (1938).
8. Webster, L. T. and Dawson, Jr., J. R.: *Proc. Soc. Exper. Biol. and Med. 32*:570 (1935).
9. U. S. Postal Laws and Regulations, 1932.
10. Railway Express Agency, Traffic Rules and Instructions, Jan. 1, 1935. *General Circular, No. 1-B*, p. 4.
11. Babes, V.: *Virchow Arch. f. Path. Anat. 110*: 526 (1887).
12. Kraus: Gerlach and Schweinburg: Lyssa bei Mench und Tier. Urban and Schwarzemberg. 1926.
13. Kracke, R. R. and Parker, F. P.: A Textbook of Clinical Pathology, 2nd ed. The Williams and Wilkins Co., Baltimore, Md. 1940.
14. Stimson, A. M.: *Hyg. Lab. Bul.* No. 65 (1910).
15. *J.A.M.A. 115*:1109 (1940).
16. Zagarro, cited by Rosenau, M. J.: Preventive Medicine and Hygiene, 6th ed. D. Appleton-Century Co., New York, N. Y. 1935.
17. Webster, L. T.: Rabies. The Macmillan Co., New York, N. Y. 1942.
18. Blatt, M. L.: Hoffman, S. J. and Schneider, M.: *J.A.M.A. 111*:688 (1938).
19. Mohler, J. R. in Farmers' Bul. 435. U. S. Dept. of Agriculture, Govt. Printing Office. 1911.
20. Hart, B. F. and Evans, E.: *J.A.M.A. 112*:731 (1939).
21. Beckman, H.: Treatment in General Practice 6th ed. W. B. Saunders Co., Phila., Pa. 1948.
22. Rehfuss, M. E.: Albrecht, A. K. and Price, A. H.: A Course in Practical Therapeutics. The Williams and Wilkins Co., Baltimore, Md. 1948.
23. Christopher, F.: Textbook of Surgery. W. B Saunders Co., Phila., Pa. 1939.
24. Rosenau, M. J.: Preventive Medicine and Hygiene, 6th ed. D. Appleton-Century Co., New York, N. Y. 1935.
25. Paul, J. R. in Blumer's Therapeutics of Internal Diseases. D. Appleton-Century Co., New York, N. Y. Vol. 2. 1940.
26. McMaster and Hudack: cited by Rehfuss M. E., Albrecht, A. K. and Price, A. N.: A Course in Practical Therapeutics. The Williams and Wilkins Co., Baltimore, Md. 1948.
27. Shaughnessy, H. J. and Zichis, J.: *J.A.M.A. 123*:528 (1943).
28. *J.A.M.A. 112*:1283 (1939).
29. Kellogg, W. H.: *J.A.M.A. 114*:910 (1940).
30. McKendrick, A. G.: *Quart. Bull. Health Organ. League of Nations 3*:613 (1934).
31. McKendrick, A. G.: *Quart. Bull. Health Organ. League of Nations* 9:31 (1940).
32. Denison, G. A. and Dowling, J. D.: *J.A.M.A. 113*:390 (1939).
33. Webster, L. T.: *Am. J. Pub. Health 31*:57 (1941).
34. Webster, L. T.: *New England J. Med. 217*: 687 (1937).
35. Remlinger, P. and Bailly, J.: *Compt. rend. Soc. de biol.* 106:523 (1931).
36. Kohn-Richards, R.: through Beckman, H.: Treatment in General Practice, 6th ed. W. B. Saunders Co., Phila., Pa. 1948.
37. Morse, M. E.: Frobisher, Jr., M. and Rabin, C. B.: Microbiology and Pathology for Nurses. W. B. Saunders Co., Phila., Pa. 1942.
38. McCoy, G. W.: *Pub. Health Rep. 45*:1888 (1930).
38a. McKendrick, A. G.: cited by Van Rooyen, C. E. and Rhodes, A. J.: Virus Diseases of Man. Oxford University Press, London. 1940.
38b. Cornwall, J. W.: *Indian J. Med. Res. 6*:237 (1918).
38c. Foshay, L.: *J. of Med. 15*:68 (1934). Discussion.
38d. Schwentker, F. F. and Rivers, T. M.: *J. Exper. Med. 60*:539 (1934).
38e. Horack, H. M.: *Amer. J. Med. Sci. 197*:672 (1939).
38f. Pickar, D. N. and Kramer, H. M.: *South. Med. J. 42*:127 (1949).
38g. Habel, K.: *Pub. Health Rep. 60*:543 (1945).
39. Rosenau, M. J.: New England J. Med. 198: 787 (1928).
40. *J.A.M.A. 115*:1109 (1940).
41. Johnson, H. N. and Leach, C. N.: *Am. J. Pub. health 32*:176 (1942).
42. Casulo, J.: *Ann. Int. Med. 23*:74 (1945).
43. *J.A.M.A. 133*:116 (1947).
44. Molina, A.: *Bol. Soc. Brasilera de Med. Vet. 8*:103 (1938).
45. Park, W. H.: Public Health and Hygiene, 2nd ed. Lea and Febiger, Phila., Pa. 1928.
46. Ravenel, M. P. in Osler and McCrae's Modern Medicine, 3rd ed. Lea and Febiger, Phila., Pa. Vol. I. 1925.
47. Williams, A. W. in Nelson Loose-Leaf Living Medicine. Thomas Nelson and Sons, New York, N. Y. Vol. 2. 1923.

Hepatitis

A Review of the Present Concepts of Inflammatory Diseases of the Liver

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Introduction

Although the liver appears to be a very simply constructed organ, its multiplicity of functions and tremendous reserve are remarkable. It is these two factors which make the study of abnormal (or normal) hepatic physiology so difficult, and explain why most of the work in this field has been dependent upon inferential conclusions from the "liver function tests," many of whose basic mechanisms have not yet been established. The frequent dissociation of the liver functions prevents any single test from being representative of the whole organ's state, as has already been made apparent by animal and human experiments. The following discussion will place emphasis upon the actual liver activity in the more acute pathological conditions, and the subject will at times be extended to envelop certain exemplary clinical manifestations currently accepted as being related to fairly specific types of hepatic dysfunction.

Liver Physiology:

A brief statement of the liver functions collected into their chief divisions is illustrative of the extensive nature of hepatic physiology.

1. *SECRETORY* (Cholegenesis)
2. *METABOLIC*
   Carbohydrate metabolism.
   Protein metabolism.
   1. Deamination.
   2. Synthesis of amino acids, uric acid and urea.
   3. Formation of antitoxic and protective substances.
   4. Formation of Vitamin A from carotene, hormone synthesis, (estrogen), etc.

   Fat metabolism.
   Mineral metabolism and acid base regulation.
   Water metabolism.
   Heat and vitamin production.
3. *STORAGE*
   Vitamin, iron, copper, hematopoietic principle.
4. *DETOXIFICATION*
5. *SCAVENGER* (reticuloendothelial system)
6. *BLOOD COAGULATION*
   Fibrinogen, prothrombin, heparin, etc.
7. *BLOOD FORMATION* (Embryonic)
8. *REGULATION OF BLOOD VOLUME*
9. *FUNCTION OF REGENERATION*

Function Tests

Since the following discussion will occasionally deal with function tests, a brief statement of the processes being measured would be helpful:

1. *Cephalin-cholesterol flocculation test:* Sera from patients with hepatic diseases are flocculated by a colloidal suspension of cephalin-cholesterol complex. (Infectious hepatitis gives the highest percentage of positive reactions and the test is positive early in the disease, in the pre-icteric phase.)
2. *Thymol turbidity test:* Sera of persons with liver disease when added to a thymol solution become turbid. (The test becomes positive after 5-7 days of hepatitis and remains positive

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longer than the cephalin flocculation test and is therefore of prognostic value.)

3. *Hippuric acid test:* Measures the efficiency of the liver's detoxifying ability in the synthesis of glycine and its conjugation with benzoic acid, to form hippuric acid.
4. *Bromsulphalein test (and other dye tests):* Measures the ability of the reticuloendothelial system to fix a foreign dye.
5. *Azorubin S test:* Measures the ability to excrete foreign dye into the bile.
6. *Bilirubin excretion test:* Measures the ability to excrete a normal constituent into the bile.
7. *The lactose and glucose tolerance tests:* Assays the glycogenic enzyme system activity.
8. *Amino acid test:* An index of the deaminifying power.
9. *Prothrombin response to Vitamin K, A-G ratio, and cholesterol ester determinations:* Measure the power of synthesis of the liver.
10. *Glycogen storage test:* An appraisal of the glycogen stores and glycogenolysis.

There are many other tests which will not be elaborated upon.

Hepatic Insufficiency

In analyzing liver failure, it is important to keep in mind certain considerations:

1. Reduction in hepatic function is not symmetric; dissociation is the rule.
2. Hepatic insufficiency can exist without demonstrable histologic evidence. (This is a limiting factor in the interpretation of liver biopsies.)
3. Hepatic reserve allows destruction of a major fraction of the cells without insufficiency, but relatively minor damage involving all of the cells' impairs efficient function.
4. Clinically the symptoms of this state may persist long after the biochemical evidence of disease has gone; hepatosplenomegaly may persist after both symptoms and impaired function are no longer apparent.

In the consideration of acute liver abnormality, the most important type of hepatic insufficiency is parenchymatous in origin. However, it is not always easy to separate this from those forms resulting from circulatory changes in the liver or from biliary duct dysfunction. The circulatory role is of greater importance in the chronic cirrhoses and in the surgical procedures pertaining to the hepatic and biliary systems.

The grades of functional failure are of importance in prognosis and treatment and in understanding the sequence of impaired liver activity. In the early stages of failure, the following changes occur:

1. Bile salt synthesis, reclamation, conjugation and destruction may be impaired early.
2. A rise of serum bilirubin does not occur immediately, but if it is injected, thereby placing a load on the excretory mechanism of the hepatic cell, a rise may result. (The bilirubin excretion test, therefore, may be positive in early failure.)
3. The excretion of foreign dyes and pigments is impaired. This fact explains the requirement that liver function must be normal to accurately interpret the cholecystogram.
4. Early changes occur in the various plasma proteins. These alterations are the factors producing positive reactions of the cephalin-cholesterol flocculation, thymol turbidity, colloidal gold, Takata-Ara, and other similar tests.
5. Synthesis of glycine is diminished and this is apparent in the hippuric acid test. It has been shown that it is the rate of glycine synthesis and not its conjugation with benzoic acid that actually determines the result. There is some doubt as to the complete reliability of this test, since part of the benzoic acid may be conjugated with glycuronic acid.
6. Glycuronic acid synthesis is also diminished and this substance is essential in the process of detoxification, as it conjugates with alcohols, alkaloids, etc.

7. Glycogen storage is diminished. Lactate normally is readily converted to glycogen, but if an excess is injected in mild insufficiency of the liver, the blood level rises. In advanced cases the blood lactate may be elevated endogenously.
8. Detoxification of cinchophen and other substances may be impaired. In such cases oxycinchophen appears in the urine and furnishes the basis for a test of this activity.

In the intermediate stages of liver insufficiency, the following changes occur:

1. The total blood cholesterol and the cholesterol esters fall, as a rule, in this stage, but this may occur earlier.
2. The liver cells become unable to use Vitamin K in the formation of prothrombin and consequently there is little response to the administration of this vitamin.
3. Alkaline phosphatase normally is excreted into the bile and its level may be slightly elevated in parenchymal damage. Occasionally the rise is so great in obstructive jaundice that an increased hepatic production must play a role.
4. Carotene conversion to Vitamin A decline. Blood levels and dark adaptation may be reduced. Thiamin and ascorbic acid storage is probably also decreased.
5. Water balance is often upset. This point will be discussed later.
6. The liver and carbohydrate metabolism has already been mentioned, but it should be noted that every case of chronic hypoglycemia should be studied for hepatic dysfunction. Infectious hepatitis, especially with ascending cholangitis, has produced hypoglycemia with collapse quite frequently. Glucose tolerance tests may be informative. Such patients are better treated with a high protein intake than by attempting to maintain a high blood sugar level by administering carbohydrates.
7. Estrogen destruction in the liver is decreased, which probably accounts for the gynecomastia and the testicular atrophy frequently seen.
8. Discharge of fat from the liver is impaired.

In Stage 3, or marked hepatic insufficiency, there occur:

1. Impaired electrolyte and fluid balance, as well as control of blood volume.
2. Glycogenolysis persists and the hypoglycemia appearing late is due to depletion of glycogen storage. There is alteration in the oxidation of fatty acids to ketones.
3. Deamination of amino acids may be impaired with a consequent rise in their blood level. The blood urea may decline, since the urea synthesis is entirely hepatic and ammonia from deamination is not available for its formation. This picture of hyperamino-acidemia and low blood urea nitrogen is characteristic of acute hepatic necrosis.

Although these signs of functional impairment by no means comprise a complete list of the physiopathologic changes going on in the liver, they serve to demonstrate an approximate estimate of the sequential qualitative changes in the failing liver.

Acute Liver Disease
Hepatorenal Syndrome

Sudden unexplained postoperative deaths in biliary tract surgery have been ascribed to liver dysfunction. These deaths were classed as follows:

1. The patient who is generally a "good risk" with a history of biliary tract disease, who tolerates the actual surgery well, but in whom there is a delayed recovery from the anesthetic, with subsequent development of coma, hyperpyrexia, and death, within 24 to 48 hours.
2. The jaundiced "fair to good risk" patient, who does well for 24 to 48 hours, but then becomes irritable and dies in hyperpyrexia and vasomotor collapse, within 24 to 48 hours.
3. The patient with a biliary tract infection, secondary to a stone, who is also a "fair risk" and who does well

for 5 to 6 days after surgery, at which time he becomes lethargic, oliguric, comatose and expires. This constitutes the original hepatorenal syndrome.

It may very well be that the same basic abnormal process, namely, an inherent or acquired parenchymal cell weakness (subclinical), which becomes more pronounced under the strain of surgery, occurs in all groups, and that the different stages may be part of the same basic abnormal process. It is believed that the release of a toxic substance into the blood stream from the liver results in damage to the convoluted tubules during the excretion by the kidney. Recently much work has been done on lower nephron nephrosis with particular relation to the "crush syndrome." It has been assumed that under certain circumstances, the shock of hepatic and biliary tract surgery may produce a lower nephron nephrosis.

SHOCK: The inter-relationship of the liver and kidneys in shock has recently received much attention. A vaso-exciter substance, elaborated by the kidney, has been found, and a vasodepressor substance, elaborated by the liver, has also been discovered. Each is formed anaerobically and destroyed in its respective organs aerobically. In shock the vaso-exciter substance enhances adrenalin action on the terminal vascular bed at first; later the vasodepressor substance becomes dominant and produces the opposite effect. The anoxic liver in shock inadequately inactivates the vasodepressor substance, resulting in an eventual irreversible depression of the vascular bed, with collapse. It is in this stage of shock that transfusions may be of no value.

It has been emphasized that there is a definite increase in the frequency of renal sulfonamide complications in patients with diffuse liver impairment. These complications are even more frequent if the liver is injured by the sulfonamide. This should serve as a warning when using sulfa drugs in the presence of hepatic disease.

Hepatic Coma

Although hepatic coma is not uncommon, the mechanism of its occurrence is poorly understood. Clinically the signs of nervous irritability, occasionally reaching the point of generalized convulsions, with frequent oliguria, and anuria in the late stages, are frequently seen. It is assumed that the cause of hepatic coma is an impairment of the intermediary glucose metabolism by interference with the action of the enzyme systems. It has been suggested that cerebral edema is the immediate cause of the symptomatology and that the concomitant changes in the brain cells precede the blood chemical abnormalities. It may be true that deaths are due to a release of hepatic toxins from hepatic cell degeneration.

Infectious Hepatitis

The recent war, with its epidemics of jaundice, provided a great impetus to the study of the more acute liver diseases, and resulted in the clarification of many facts and the abandonment of empiric hypotheses. For many years epidemic and sporadic jaundice was termed "catarrhal jaundice," and was originally ascribed to a mucous or catarrhal inflammation of the ampulla of Vater. It is now recognized that this condition is an extreme rarity, only three cases having been proved, and that the true nature of the pathology is one of acute diffuse parenchymatous disease. The entity of acute viral hepatitis and homologous serum jaundice is well known and in spite of much work being done in this field, there is a surprising lack of information concerning the etiologic factors and the abnormal behavior of the damaged liver cell itself.

The etiological factor in hepatitis is thought to be a virus. Virus IH, the virus of infectious hepatitis, or "catarrhal jaundice," or "hepatitis epidemica," may be transmitted by respiratory secretions, sewage (with flies as vectors) or through infected food and water or direct transmission. The incubation period ranges from two to six weeks. Virus SH, the factor of homologous serum hepatitis, is probably identical with the factor of "transfusion jaundice," "postvaccinal or vaccinal jaundice or hepatitis," "post-

inoculation hepatitis," "syringe hepatitis," and probably so-called "late post-arsphena mine jaundice." The incubation period for this entity is longer, one to six months.

The morbidity rate is high; in some of the epidemics among troops, 40-65 per cent of the personnel were afflicted. Due to the relatively prolonged period of disability (the average is sixty days), it was the greatest cause of disabling illness (greater than malaria).

The mortality varies from 0.2 per cent on an average to 6-19 per cent for some smaller outbreaks. On the whole, the mortality of serum hepatitis is higher than infectious hepatitis.

Prophylaxis: There is no known method of active immunization against infectious hepatitis although passive immunization of individuals exposed to the disease by intramuscular injection of gamma globulin can be expected to offer some protection, and is advisable in the presence of an epidemic.

Physiopathology: In the typical epidemic or sporadic form of the disease, the pathological picture has been described as damaged hepatic cells, periportal inflammatory exudation, and occasional necrosis of the cells in the periphery of the lobule. The importance of composite liver function studies is perhaps nowhere of greater importance than in cases of acute hepatitis. The usual form of the disease is that of primary hepatocellular damage and dysfunction, although this can rarely be completely separated from cholangiolar derangement, which will be spoken of later.

The principal laboratory evidences of hepatocellular dysfunction are:

1. Increased delayed reacting bilirubin
2. Increased urinary urobilinogen
3. Diminished galactose clearance
4. Diminished hippuric acid synthesis
5. Diminished serum albumin
6. Diminished cholesterol ester fraction
7. Positive cephalin-cholesterol flocculation
8. Positive thymol turbidity

It is important again to emphasize that dissociation of any of these may occur, requiring a fairly complete survey to create a true functional picture. This group of tests may be as indicated in the absence of jaundice, which clinical entity may appear infrequently in some epidemics, making the diagnosis most difficult. Many cases of hepatitis without jaundice have been accused of malingering and frequent diagnoses of neurosis, etc., have been made. Bilirubinuria in hepatitis commonly precedes the appearance of clinical jaundice, often before the serum bilirubin is appreciably elevated. There seems to be a change in the renal threshold to bilirubin during the course of the disease, for eventually there may be cessation of biliuria when the serum bilirubin level is still elevated. This is a practical consideration to be kept in mind when following patients clinically.

Quantitative urobilinogen determinations are of great value in hepatitis. Typically there is an early pre-icteric elevation, which may occur though jaundice never does appear. The amount often fluctuates from day to day, and may disappear at the peak of jaundice, only to return after a few days, thereby marking the onset of rapid improvement. It has been shown that serial quantitative urobilinogen levels is the test least likely to give normal results in icteric hepatitis, and most likely to give abnormal results after jaundice has subsided. Persistence of a positive test indicates a continuance of the activity of the process, and this test may therefore be used as a prognostic index in convalescence.

The cholesterol ester fraction characteristically is low in hepatocellular disease, but it may also be depressed after prolonged biliary obstruction, although this does not occur in the early stages of obstruction of the common bile duct from stone, pancreatic carcinoma, etc. (Early in obstruction it may be high and aid in the differential diagnosis of jaundice.)

Bromsulfalein retention occurs early in hepatitis and rapidly becomes pronounced. Persistent elevation after the cessation of jaundice suggests continuing activity and the possibility of early cirrhosis.

The cephalin-cholesterol flocculation and thymol turbidity tests agree well in hepatitis, probably better than in chronic liver abnormalities. The cephalin test generally

becomes positive earlier than the thymol. However, the latter may remain positive for a longer period of time.

The liver function tests of greatest value in the practical study of hepatitis are as follows:

1. The pre-icteric stage
   a. Serum - bilirubin (especially the prompt reacting type)
   b. Urine bilirubin
   c. *Urine Urobilinogen*
2. The Icteric stage
   a. *Cephalin-cholesterol flocculation*
   b. Thymol turbidity
   c. Serum cholesterol and cholesterol ester ratio
   d. Serial urine urobilinogen
   e. Serum alkaline phosphatase—(aids in differentiation from obstructive jaundice).
3. Defervescent stage
   a. Serum bilirubin (especially the delayed reacting type)
   b. Urine urobilinogen
   c. Thymol and cephalin tests
   d. *Bromsulfalein excretion*
   e. Urinary coproporphyrins

It has been shown recently that the 24-hour excretion of coproporphyrins is a valuable test of latent liver damage, residual or chronic hepatitis, and early cirrhosis. The level is elevated in hepatitis, even when the other tests have returned to normal. The test, however, is of little value diagnostically in the presence of any regurgitation jaundice.

Alterations in the water metabolism in hepatitis have recently been studied. Careful measurements and controls revealed an early increase of blood and plasma volume; decrease in plasma and urinary chlorides; and an increased retention of ingested water. At the onset of convalescence there is usually a marked and definite diuresis. Bio-assay of the excretion of an antidiuretic principle in these patients revealed high levels early in the disease with a fairly prompt fall at the onset of convalescence.

Homologous Serum Jaundice (Transfusion jaundice, etc.)

The pathologic physiology of this condition is very similar to that already described in epidemic hepatitis. The differences are in the virus strains, portal of entry, prognosis and several other factors.

Because of the slight, but definite, risk of hepatitis, the use of blood, plasma, or substances containing blood, should be restricted to patients whose need is definite, and in whom the indication will outweigh the risk. Methods for control of the virus in plasma or blood are now in use.

Cholangiolitic Hepatitis

This is a less common, but more severe form of hepatitis, characterized by evidence of prolonged intrahepatic biliary block, with severe jaundice, frequent hepatosplenomegaly, and a high mortality. These cases present difficult diagnostic problems, since they may imitate extrahepatic biliary obstruction. There is apparently an increased permeability of the cholangioles with a resultant leakage of the bile therefrom. It is suggested that these cases begin as a hepatocellular form of the disease, which has undergone partial repair at the time the cholangiole damage becomes apparent.

The principal evidences of cholangiole dysfunction are:

1. Increased prompt reacting bilirubin
2. Bilirubinuria
3. Bile salts in the blood and urine (often resulting in pruritus)
4. Increased total blood cholesterol
5. Increased serum alkaline phosphatase

Acute Atrophy of the Liver

This is not actually a disease entity, but rather a fairly rapid generalized necrosis of the hepatic cells resulting from some insult such as hepatitis, toxic agents, or various systemic infections. Often the precipitating factor appears to be relatively trivial, but this apparently is a "trigger" mechanism flaring up a previously damaged liver. This process is the cause of death in many fatal cases of hepatitis. The liver appears to shrink, but this is due to an actual destruction of the liver rather than a true atrophy.

Chronic Hepatitis

It has been shown that acute infectious hepatitis and homologous serum hepatitis may be followed by a prolonged period of disability with or without other evidence of persistent hepatic disturbance. "Chronic hepatitis" is the term applied to cases in which the clinical manifestations or laboratory evidence of active hepatitis persist for four months or more after the onset of the initial infection. Approximately twenty per cent of infectious hepatitis cases become chronic.

Some of these patients have no jaundice, and present a difficult problem in diagnosis and management. Most of the hepatic function tests in common use are normal, including the cephalin-flocculation test. Serial liver biopsies show the lesion to be a periportal inflammation without any other significant abnormalities.

The principal positive findings are enlargement and tenderness of the liver, slight elevation of the serum bilirubin or icterus index, retention of bromsulfalein and positive histologic changes as demonstrated by needle biopsy. Less frequently there may be an elevation of the sedimentation rate, prolonged prothrombin time, and sometimes a positive cephalin-flocculation test.

Most of the patients recover after one year. However, one case died of portal-cirrhosis after three years, and another case has been reported which showed persistent liver damage after 25 months. Intermittent bilirubinemia may be present after one to two years. Portal cirrhosis is a rare sequel of infectious hepatitis.

Characteristically these patients complain of easy fatigue, anorexia, right upper quadrant pain, and enlarged and tender livers. The only factor which appears to play significant roles in the incidence of residuals, is the severity of the jaundice at the onset of the acute infection; those patients having severe jaundice have a higher incidence of chronic hepatitis. It is possible for patients to relapse after an apparent recovery, as well as to fail to fully recover from the acute stage of the disease.

Cirrhosis

CLASSIFICATION—

A. Portal cirrhosis

1. Ordinary portal cirrhoses — large and small liver; including fatty cirrhosis
2. Post-necrotic cirrhosis (toxic cirrhosis)
3. Pigmentary cirrhosis (hemochromatosis)

B. Biliary cirrhosis

1. Primary
   a. Intrahepatic, cholangitic or cholangiolitic biliary cirrhosis
   b. Primary xanthomatous biliary cirrhosis
2. Secondary
   a. Partial obstruction of extrahepatic biliary ducts with or without infection, due to traumatic stricture of impacted gallstone.

C. Congestive cirrhosis (cardiac cirrhosis)

D. Syphilitic nodular cirrhosis

Two mechanisms are suspected in the evolution of the so-called atrophic cirrhosis from the hypertrophic forms of cirrhosis. The usual method is that in which the liver becomes fatty and injured with the development of a fatty cirrhosis secondary to malnutrition with an accompanying alcoholism. The fat is then replaced by scar tissue, with the resultant fibrosis and the production of the familiar "hobnail" liver.

The second method is related to the cholangiolitic hepatitis, eventually producing a large *non-fatty liver,* which begins with periportal lymphocytic foci, bile thrombi, bile duct proliferation, hyperplasia of reticular cells and fibrosis. Later the fibrosis continues with the resultant hardening and shrinking. The cholangiolitic type of hypertrophic cirrhosis is believed to be a distinct entity and perhaps is the same as the so-called Hanot's hypertrophic biliary cirrhosis. These patients have a regurgitation jaundice without ascites, with pruritus, hypercholesterolemia and hyperphosphatemia. The end stages of the "hobnail" atrophic cirrhosis produced by either of these entities may be indistinguishable.

In Laennec's cirrhosis the serum globulins are elevated, particularly the euglobulin. A fall in the serum albumin frequently accentuated by a rise in the serum globulin is characteristic of a disturbance in the parenchyma of the liver. (Recently the 13½ per cent fraction of the euglobulin has come into prominence. In acute cases of parenchymal hepatitis, this abnormal fraction quickly disappears on recovery. It is not present in normal patients' serum.)

Endocrine changes have been noted to be associated with cirrhosis of the liver. The development of gynecomastia in the male is not uncommon. In cirrhotics about 85 per cent of injected estrogen is recovered in the urine and in patients with severe liver failure, the major part was not conjugated but in the free form. The female with cirrhosis frequently has a menstrual disorder. Testicular atrophy has frequently been described in patients with severe cirrhosis and has been aggravated by hormonal injections. (There is good evidence that the normal liver conjugates and detoxifies the estrogens.) Cirrhotic males frequently complain of decreased libido and potency, decrease in body hair and gynecomastia. Abnormal menstrual patterns are frequently found in cirrhotic females. Telangiectasia is common.

Signs and Symptoms of Hepatitis

It is possible for the patient with an infectious hepatitis to present nothing but a yellow tint to the skin, and there may be no pain or distress. However, the commonest symptoms are malaise, easy fatigability, anorexia, headaches, occasional nausea or vomiting, and an uneasy feeling in the right upper quadrant. Fever, sudden in onset, with occasional chills, occurs early in infectious hepatitis, but need not be present. The pulse may be normal or slow and may fall to a rate of 30 to 40 per minute and the respirations may also be reduced. A feeling of depression is common, as well as lethargy.

Physical examination reveals little else than an icteric tint to sclera and skin and an enlarged and tender liver with a smooth, firm border. Spider angiomata may occur over the abdomen and on the face. (These disappear in a few months.) The spleen may be increased in size, and there may be lymphadenopathy.

The stools usually become light or clay colored, and the urine contains an increase in bile pigment.

The blood count is often normal, but there may be a leukopenia and a lymphocytosis. If there is much active destruction of the liver, the white blood count may become slightly elevated, and there may be an increase in nucleated cells.

Treatment

There is no specific therapy for liver disease; it is mainly supportive. Dietary, as well as parenteral, therapy consists of a high carbohydrate, high protein, high vitamin regimen. (Fats are restricted.) The diet should be soft, bland, and easily assimilable. The fluid intake should be high and often supplemented with intravenous glucose (20 per cent). If the albumin-globulin ratio is much disturbed, parenteral protein should be administered, either in the form of amino acids, plasma, or blood. Vitamin K. B Complex, and Vitamin C are indicated. Inasmuch as there may be failure of intestinal absorption, parenteral administration is advised.

The liver diet consists of protein, 150 grams, carbohydrate, 350 grams, and fat 100 grams, a total of 2900 calories. A valuable supplementary feeding consists of fortified milk powder and milk. (1000 calories to the liter.) This enriched milk powder is given hourly in acute cases and occasionally one to three units of insulin per gram of glucose is administered.

If liver damage is diffuse and severe, concentrated liver extract intramuscularly is indicated. Mixtures of choline and cysteine are also advised. Choline reduces the incidence of posthepatic cirrhosis. Its action is lipotropic and prevents the deposition of fat in the liver. (In dogs with induced hepatitis from CCl_4, TNT, etc., it has been shown to be particularly helpful.)

Methionine aids in the production of choline. The amino acid, cysteine, may be

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CASE REPORTS

The Status of Aureomycin in Rocky Mountain Spotted Fever and Common Infections

Crispin Cooke, M.D.
Huntington, N. Y.

An attempt to cover all phases of the rapidly accumulating knowledge about Aureomycin would consume far more time and space than is available and the choice of the title of this paper is meant to imply an attempt to bring up to date the status of the drug only in those diseases which we are apt to see in this part of the country. I shall mention only briefly its effect against infectious agents rarely present here, such as typhus or typhoid, important as these may be elsewhere.

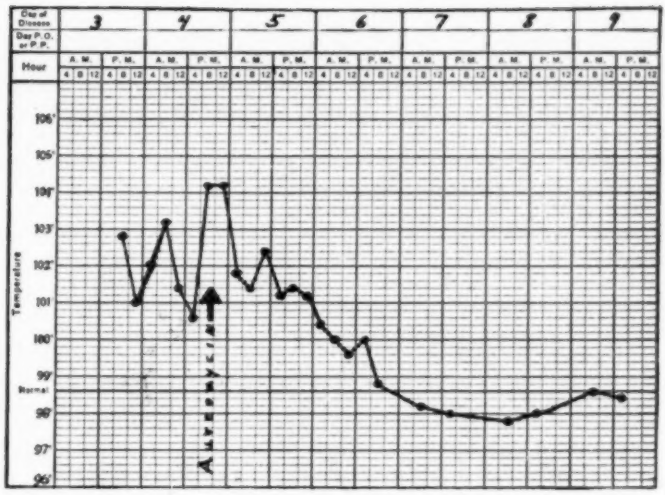
As a springboard for our discussion I wish to review briefly its effect in a case of Rocky Mountain Spotted Fever, not for the sake of outlining the features of this disease, but because the result in this patient seems to be in every way the prototype of the result in many different febrile illnesses so treated.

A twenty-eight-year-old woman was admitted to the Huntington Hospital in July, 1948, with a three-day history of headache, malaise and backache of sudden onset. Two weeks previously she had pulled two imbedded ticks from her body. On admission she had a temperature of 103 F. and the pink macular rash typically distributed centrifugally on the legs and arms. There were no other physical findings of note and the spleen was not palpable. At this time there was nothing diagnostic about her laboratory work as one would expect. The clinical impression of rocky mountain spotted fever was later confirmed by positive complement-fixation tests in high dilution, done by Doctor Cox at the Lederle Laboratories. Through Doctor Yale Kneeland, at the Presbyterian Hospital, we were fortunately able to obtain an experimental supply of Aureomycin. Treatment began on the fourth day of the illness with one gram every six hours until the temperature had dropped and then one-half gram every six hours for twenty-four hours longer, making a total of ten grams. This produced a dramatic fall in her fever as you may see from her temperature chart, and an equally satisfactory subsidence of her symptoms and signs in forty-eight hours.

Since that time a great many cases have been reported by different groups, all with equally good results, though not more so than with Chloromycetin. With the exception of the recent Rickettsial pox outbreak on Long Island, this is the only Rickettsial disease which we are apt to see. However, Aureomycin has effectively controlled epidemic and murine typhus, scrub-typhus, Q fever and all the known Rickettsial diseases on which it is known to have been used.

To turn to the pneumonias, which are perhaps the commonest severe infectious problem that we face, I am sure that all of you have used Aureomycin in atypical or so-called virus pneumonia and are as familiar as I with the several series of cases so successfully treated by Doctors Finland, Kneeland and Rose, and others. Its usefulness in pneumococcal pneumonia is perhaps less well known. The sensitivity of pneumococci to the drug has been long established and Doctor Finland reported four cases with prompt response at the Symposium of the New York Academy of Sciences on Aureomycin a year ago, and others have been reported since. Recently

Read before the Scientific Session of the Associated Physicians of Long Island held in the Huntington Hospital, Huntington, N. Y., on June 21st, 1949.



we have had a patient with a typical lobar pneumonia due to a type IV pneumococcus with a positive blood culture, who was sensitive to both sulfonamides and penicillin. On Aureomycin she had a response in every way comparable to that to be expected from the more usual antibiotics, and a temperature curve which could almost be superimposed on the case of Rocky Mountain Spotted Fever just shown. Doctor Kneeland has told me of one or two treatment failures in lobar pneumonia of pneumococcal origin at the Presbyterian Hospital, so that penicillin is still of course the drug of choice. Under such circumstances as the above case, however, it may be well to consider the use of Aureomycin. The remarkably wide spectrum of activity of this drug is of course an asset, but as pointed out recently to me by Doctor Walsh McDermott, this should not lead us into treating every case of pneumonia blindly, with this drug or penicillin either for that matter. The most serious common pitfall in not doing sputum cultures, and making every attempt to find out the etiology of a pneumonia, is the failure to identify a Friedländer's bacillus infection. It is variously estimated that in different years one or two cases per one hundred of lobar pneumonia in any large series will be due to Friedländer's bacillus, with an untreated mortality rate of eighty to ninety per cent and a very high morbidity of chronic pulmonary invalidism in those who do recover. This organism is insensitive to penicillin and strains vary greatly in their resistance to Aureomycin, whereas Sulfadiazine and Streptomycin combined are still the drugs of choice in preventing the rapidly necrotizing pulmonary infection of a Friedländer's bacillus, if they are given early. If one waits for several days before instituting the correct treatment, the lung may have been irreparably damaged.

Another frequent entity we all face is that of resistant urinary tract infections, usually due to gram-negative organisms. A recent report in the proceedings of the Society for Experimental Biology and Medicine shows that there are wide variations in sensitivity of strains of given species of *B. proteus, B. coli, A. aerogenes* and *pyocyanens,* which are the common offenders. In their series, it was possible to sterilize the urine in three of four patients with a univalent infection and five out of six patients with a polyvalent infection in whom other antibiotics had been unavailing. It is to be noted, however, that these cases were not complicated by hydronephrosis, etc., as were those of Doctor Finland, previously reported, where results were less good. In general, one may say that strains of *B. proteus* and *pyocyanens* which are sensitive in vitro may be eliminated, but that if insensitive, these strains will overgrow the Coli-Aerogenes group under treatment with Aureomycin. It is therefore important to determine strain of sensitivity whenever this is possible.

One other fairly frequent disease which we all see, and on which I can touch only briefly, is brucellosis. It must suffice to say from the published experiences of Doctors Spink, Doctor Perrin Long and of Doctors Knight and McDermott, that in general, acute cases of undulant fever due both to the melitensis and abortus strains show a remarkably good and sustained response, whereas the chronic cases do not do so well. Experimentally Aureomycin does not eliminate brucella in the spleens of infected mice and the final chapter is still to be written. Yet it is probably our best agent to date.

The lack of toxicity of this drug, aside from the nausea and vomiting, which many feel is helped by the use of Amphojel, and the lack of development of bacterial resistance at least relative to that seen in other antibiotics, as far as now known, are among the great advantages of this drug. Methods of bio-assay are not entirely satisfactory but its effective urine and blood concentration is well known and apparently easily held by administration every six to eight hours. No good parenteral preparation is as yet available and even when it is given in Procaine it is still very painful and usually not necessary. It has been reported present in the cerebrospinal fluid in most patients tested who were on an adequate dose. It has not been shown that there is any cross resistance developed by organisms resistant to Penicillin, Streptomycin, Bacitracin or Polymixin. It is to be supposed that the great objection of its high price will rapidly be solved by better production methods.

I have listed a table of its antimicrobial activity as I have been able to determine it from the literature. Lack of time prevents me from commenting on this, but I felt that it might answer some of your questions to have this as a sort of summary. I must make the reservation that it is incomplete and that many of these findings are based on preliminary reports and may have to be changed as experience accumulates. In closing I should like to paraphrase what Doctor Goldstein said in his review of Antibacterial Chemotherapy, in the *New England Journal of Medicine*, this year; that as to the clinician these antibiotics give a weapon against disease, so to the laboratory investigator they furnish tools for probing the mechanisms of cell life. None less than Paul Erlich, many years ago, said in part: "I am of the opinion that the fundamental question of pharmacology, the question of combinations of drugs and the cause of such combinations, will hardly be brought to a solution in the complicated higher organism; rather it is more to the point to study such processes in their purest cellular form in the simplest of cells." In the furthering of the solution of this basic problem from which we will all gain so much, Aureomycin is another of the extraordinary discoveries of the past decade.

Discussion by Elmer H. Loughlin, M.D.

Doctor Cooke in his paper on The Status of Aureomycin in Rocky Mountain Spotted Fever and Other Common Diseases has given an extremely clear as well as concise presentation of a relatively new antibiotic, Aureomycin, which has been found effective in certain infectious diseases hitherto unresponsive to other antibiotics and chemotherapeutic substances.

In Brooklyn we have had considerably less opportunity than Doctor Cooke to encounter cases of Rocky Mountain spotted fever, so that any opinions which I might hold on this disease treated with Aureomycin obviously would be dependent upon the observations of such workers as Doctor Cooke.

Contrarywise, we encounter a fair number of cases of atypical pneumonias, and these have responded in an almost uniform fashion to therapy with Aureomycin. In these pneumonias, however, we attempt to administer initially a series of "loading" doses which, in adults, ranges from 250 mg. to 500 mg. every hour for three doses, then 250 mg. to 500 mg. every two or three hours until the temperature has returned to normal, then 250 mg. every four to six hours for two to five days until convalescence is well established. Reports are available where Aureomycin has been found to be extremely effective in the treatment of tularemia. We have

A Partial List of Aureomycin Effect

Infectious Disease or agent	*Effective*	*Comment*
Streptococci—	Yes	No better than usual antibiotics except on S. fecalis.
Staphylococci—	Yes	Excellent results in furunculosis.
Pneumococci—	Yes	Probably equal to usual agents.
Meningococci—	Yes	No clinical reports except in meningococcemia.
Gonococci—	Moderate	Not so good as usual agents.
Brucellosis—	Yes	Excellent in acute Melitensis and Abortus; less so in chronic cases.
Tularemia—	Yes	Good clinical results.
B. Typhosus—	Poor	Chloromycetin far superior.
Salmonella—	Poor	Chloromycetin far superior.
E. Coli—	Variable	Marked strain variability.
B. Proteus—	Variable	Marked strain variability.
Pyocyaneus—	Poor	Marked strain variability.
A. Aerogenes	Variable	Marked strain variability.
Tuberculosis	No	No activity in the guinea pig.
Rickettsia—	Yes	Against all known types treated.
Spirochetes—	Probable	Experimentally vs. relapsing fever, Weil's Disease and [?] T. Pallidum.
Viruses—	Variable	No effect vs. most in vivo or vitro, as Influenza, Poliomyelitis, Mumps, Rabies.
Atypical Pneumonia—	Yes	Several series reported.
Lymphogranuloma—	Yes[?]	Acute process subsides; recent reports less favorable.
Granuloma Inguinale	Yes[?]	Only a few cases reported.

had no personal experience with Aureomycin in the treatment of this disease.

With brucella infections a somewhat different method of administration must be considered since in these infections treated with Aureomycin so-called Herxheimer's reactions occur when standard doses of this antibiotic are given. It is, therefore, necessary to begin therapy for the first day or two with considerably smaller doses and then, provided no reaction has occurred, to give the usual full doses.

A helpful measure which may be used during this preliminary phase of therapy to avoid such reactions is the simultaneous use of either Benadryl or Pyribenzamine.

I again compliment Doctor Cooke on this fine presentation of a very important subject.

✚

CANCER RESEARCH

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fragments if one dried them. If they do not disintegrate, our present ideas about cells are all wrong. Pathologists would never seriously consider the possibility of abandoning their established notions on this matter, if the alternative were not to throw overboard their even more deeply ingrained ideas of the nature of cancer.

(iii) Any important discovery becomes doubly and trebly convincing when the work can be repeated in other laboratories.

Why is it important to settle if viruses cause cancer? Will it help us to prevent or cure cancer? The answer is that, even if we cannot see far ahead, understanding of cause must ultimately help towards successful prevention and cure. Any advances in the difficult field of virus chemotherapy, for instance, will seem more likely to be applicable in the future to cancer. More immediately important, an enormous amount of current research work on the cause of cancer can be discarded as unprofitable; and workers' efforts can be directed to following up this new lead, and new lines of work which it suggests.

One thing should be realized. Because a parasitic virus causes cancer, it does not follow that cancer is an infectious disease like measles; indeed, we know it is not. There are plenty of other parasitic diseases which are highly conditioned; that is, the parasite may be there, even within the "host" or victim, but no disease will be caused until other conditions are fulfilled. Many people have the virus of herpes simplex or fever-blisters always present in their tissues; the eruption only occurs, however, when a cold or some other stimulus upsets a balance between them and their tame virus. So, too, there may be a "sleeping" cancer virus in mice, doing no harm until x-rays or tar upset a

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CASE REPORTS

Recovery from Pemphigus Treated with Aureomycin

Adolph L. Natenshon, M.D.
Milwaukee, Wisconsin

History

In January, 1949, Mr. P. B., aged sixty-seven years, a laborer in a paint factory, noticed a rash on both hands which itched constantly. The rash then spread to the extensor surfaces of both forearms. After five or six days, the rash occurred on the feet, legs, and in the groins. The rash, which consisted of tiny papules, itched so much that he kept scratching until they suppurated and the skin became red and swollen.

He was seen by a physician who diagnosed scabies, prescribed sulfur, and the condition got much worse. A second physician then treated him with lotions and baths, with some temporary relief.

On February 3, 1949, the patient was seen in this office. A complete physical was done, and a diagnosis of contact dermatitis, anemia, varicose veins and chronic gallbladder disease was made. The rash resembled scabies, and had a similar distribution over the body. At the time, it was felt that woolen underwear might be the cause of his dermatitis, so he was advised to change to cotton underwear. He was treated with lotions and wet compresses, but did not tolerate oatmeal baths. The patient responded quite well to treatment; the rash clearing up over the weekends, but reoccurring on returning to work.

He was employed at a large paint concern for years, and his work consisted of removing paints off of metal slabs. Patch tests were done with "thinners" and "dust" materials used in his work, and within ten minutes were positive to such a degree that the material had to be removed at once. The company dermatologist then treated him for industrial dermatitis for about a week, and his legs became so bad it was necessary to hospitalize him.

Ten or twelve days after admission into the hospital, he developed what was thought to be erythema multiforme. After five weeks of treatment consisting of penicillin, baths, lotions and liver injections, the patient became progressively worse. He became irrational, couldn't eat, and lost twenty-five pounds in weight. He ran a septic temperature with albumin in the urine. The weakness was so great that he fell over several times in a day.

On April 8, 1949, he was transferred to Mount Sinai Hospital.

Past Medical History

Pneumonia, thirty years ago. Three years ago hospitalized for coronary thrombosis. No evidence of coronary since, and x-rays at a later date revealed stones in the gallbladder.

On admission to the hospital, he complained of dull, burning pain in the legs and groins, dryness of the throat, cracking of the lips and corners of mouth and generalized itching. The entire body except the face, palms of hands and soles of feet was covered with large bullae, and the surrounding skin was red, irritated, inflamed, swollen, dry and itched a great deal. Lesions were present in the nose, mouth, pharynx and on the lips. A diagnosis of pemphigus was made by two consultants.

He was started on Stovarsol, given supportive treatment, blood transfusions, and no external treatments in the hope that

the skin would dry up some. Sulfonated oil was used to cleanse.

On April 9, 1949, the patient was still running a septic temperature, and new lesions kept cropping up daily. In view of the fact that all other types of therapy had been used without success, it was decided to start the patient on Aureomycin, as the etiology of pemphigus is unknown. He was given two 250 milligram capsules of Aureomycin every four hours with an anti-acid. There were no side effects such as heartburn or diarrhea at any time when he was on this medication.

On April 19, 1949, the patient became afebrile and remained so the remainder of the time in the hospital. Shortly after starting Aureomycin he began to feel much better, the bullae seemed to dry up, and the number of new lesions became fewer in number. Four transfusions of 500cc. each of whole blood were given on April 9, 11, 15, 22, 1949.

It is interesting to note that even after two transfusions, the red count, white count, and differential remained the same, perhaps due to the fact the patient had been on Aureomycin only a few days.

An April 13, 1949, because of the uncertainty of special tests and biopsy in pemphigus, it was decided to aspirate the bullae under aseptic technique. Fluid from the bullae showed on smears occasional clusters of gram-positive cocci or coccoids. The culture showed no growth in twenty-four hours; but after forty-eight hours, gram-positive cocci, clustered; *Staphylococcus aureus* and coagulase-positive. Streptomycin-resistant; Penicillin-resistant; Aureomycin sensitive. The Aureomycin dramatically killed off the growth in a short period of time.

On April 16, 1949, repeat aspiration of fluid from bullae showed on smear very occasional small cultures of gram-positive cocci. Culture, no growth in forty-eight hours; seventy-two hours negative. Blood culture after Aureomycin on April 16 showed no growth in forty-eight hours; seventy-two hours; four days; five days; six days; seven days; negative after nine days.

April 19, 1949, the blood culture showed no growth in twenty-four hours; forty-eight hours; seventy-two hours; four days; six days; seven days; negative after eight days. On April 19, the patient developed a large fluctuating mass the size of a hen's egg over the olecranon process of the right elbow. It was needled and about 20cc. of clear amber fluid was aspirated. The smear showed occasional paired cocci and small clusters. Culture; gram-positive cocci, clusters. *Staphylococcus aureus.*

On April 17, 1949, because of the cost of the drug and the marked improvement in the patient's condition, the Aureomycin was stopped. However, a few bullae reoccurred in the mouth and on the legs.

On April 22, he was again started on Aureomycin, one 250 milligram capsule every six hours. He complained of occasional heartburn, so anti-acid was given with the drug, and the heartburn disappeared.

May 1, 1949, he was discharged from the hospital. He ate well, had gained considerable weight, was afebrile and was

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URINE	4-9-49	4-28-49
Color	Straw	Yellow
	Cloudy	Clear
Sp. Gravity	1.022	1.021
Reaction	Acid	Acid
Albumin	0	0
Sugar	0	0
Micros.:	2-3 Leuko.	3-4 Leuko.
	Benz. o	Occ. RBC
	Few Bact.	Few Sq.

BLOOD	4-9-49	4-11-49	4-14-49	4-21-49	4-28-49
Kline		Neg			
Erythrocytes	3,830,000		3,750,000		
Hemoglobin	10 gm.		11.5 gm.	13.5 gm.	14 gm.
Color Index	0.9		1.0		
Leukocytes	15,150		15,500	13,050	12,750
% Non-segmented Polys	22		11	10	14
% Segmented Polys	49		37	59	53
% Lymphocytes	14		27	19	20
% Eosin. Poly.	14		14	8	9
% Baso. Poly.			1		1
% Monocytes	1		10	4	3

CASE REPORTS

Skin Rash from Aureomycin

Albert R. Rosanova, M.D.[1] and Edward Warszewski, M.D.[2]

Chicago, Illinois

Reactions to Aureomycin reported to date have been very few and of a mild character. They have been limited to the gastro-intestinal system and consisted of nausea, vomiting, diarrhea and cramps. These generally are relieved by giving the aureomycin in aluminum hydroxide or magnesium trisilicate preparations.

The present case is a report of a mild reaction also, but it is of a skin rash produced by the Aureomycin.

Report of Case

The patient, a white female, 62 years of age, is a nun. She was not hospitalized at any time during this treatment, although she is a clerical worker in a hospital.

On July 25, 1949 she developed a sore throat, running nose, dry cough, and sneezing. She had pain in the chest which was worse on coughing. This pain was on both right and left sides of the chest at the level of the diaphragm. She also had chills which lasted about five minutes, and a fever.

She took 3 tablets of an APC type and one tablet of aspirin in a 5-day period and continued working while trying to treat herself. She also took water in slightly greater amounts than usual.

On the 6th day of her illness (July 31st. 1949) she felt worse and sought medical aid. At this time she had a temperature of 100 degrees orally and a diffuse redness with mucus discharge of the upper respiratory passages. There were fine dry rales throughout both lung fields. No signs of consolidation were noted. Diagnosis of an acute laryngotracheobronchitis was made, and because of the 6-day duration, with no response to conservative medication, it was decided to place her on Aureomycin therapy orally, in order to try this new drug in this type of case.

Accordingly she was given Aureomycin in 50 mgm. doses every two hours. The patient took these faithfully during the daytime but she did not awaken to take them at night. She averaged about 6 doses per day making a total of 300 mgm. daily. On the morning of the third day after she had already taken a total of 13 capsules or a total does of 650 mgm. of Aureomycin, she noted an itching all over her head, feet, and the entire body. She had no rash at this time but within an hour she noted a fine red rash on her arms, chest, and shoulders.

Inspection at this time showed a fine, maculopapular, red rash. The lesions averaged about 2 to 3 mm. in diameter and the same in height. There was a small area of clear skin between each lesion. They were present on both arms, anterior and posterior surfaces of the chest, and both shoulders. No other part of the body was affected. The Aureomycin was discontinued and the itching and rash disappeared within 24 hours.

It must be stated that all signs of her upper respiratory infection had disappeared on the morning of the second day, while taking the Aureomycin, and the temperature was back to normal at this time. The cough, however, persisted for 2 weeks longer. No cough medication was given at any time.

On 8-19-'49 because of the peculiar itch and eruption that had occurred it was decided to try giving her Aureomycin again, although she felt perfectly well at this time. At 5:00 P.M. on this date she was given one capsule of Aureomycin of 50 mgm. and about 6:00 P.M. she noted the start of an itch which involved the entire

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body. There was no rash present. At 7:00 P.M. she was given a second capsule of 50 mgm. of Aureomycin. At 9:00 P.M. she got a severe generalized itch and a red, maculopapular rash similar to her previous rash. This was also confined to her arms, chest, upper back, and both shoulders. The rash started to disappear during the night and was gone at 10:00 A.M. the next morning. However, the itch persisted until 5:00 P.M. the same day. No other medication or foods to which the patient was allergic were taken during the time of this trial.

The past history is that of tonsillectomy during childhood and appendectomy at 10 years of age. The patient has never had a skin rash in her life except after taking tomato juice in large quantities. She claims that this gave her an itch and rash similar to the experience described with Aureomycin above. She had a severe bronchial infection about a year ago for which she received penicillin injections at that time.

She gives a definite history of allergy to foods. Orange juice, tomatoes, tomato juice, strawberries, lemonade, fresh honey, and raw milk always give her a diarrhea. Tomato juice in large quantities would give her also a skin rash and itch (as above stated). She did not have any of these foods or juices at any time during her illness or while taking the trial capsules of Aureomycin.

Comment

A definite skin rash with itching is noted in a patient after taking Aureomycin. The patient had a definite previous history of allergy to foods.

Summary

A case is reported showing a mild skin rash with itching as a reaction to Aureomycin. This case is reported because no other reaction of this nature to Aureomycin appears in the literature at the present time.

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RECOVERY FROM PEMPHIGUS

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up and around. The skin had cleared up, no bullae were present, and the legs, which were affected the most, were not swollen or painful.

At home he was kept on Aureomycin, one 250 milligram capsule three times daily. Over a period of two months he has used eighty capsules of Aureomycin. At present, he is taking one capsule daily for two weeks, after which the drug will be stopped entirely.

On June 17, 1949, he noted a few bullae on the feet and he felt tired. However, he had been out of medication for several weeks. His red count was 3,860,000. The patient was put on an iron and liver preparation, massive doses of B Complex and vitamin C. Only sulfonated oil was used for cleansing the skin, and no other external preparations were used.

On July 20, 1949, his weight was 160 pounds, a gain back of thirty pounds. The red count was 4,720,000, white count, 8,250. The skin was clear, and except for occasional itching, he was planning to go to work.

Conclusion

Although toxic pemphigus is not uncommon, up to the present time most of these cases have died in spite of any known therapy. This case presents a typical picture of pemphigus with a staphlococcus septicemea, and fortunately it responded to Aureomycin. Though this is only a single case study, it may help reveal the etiology of toxic pemphigus and possibly present a cure for this almost always fatal disease.

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CANCER RESEARCH

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balance between virus and cell and the cancer starts. Attention to the upsetting agent may be more practically important than attention to the virus. But the upsetting agent is not the cause: it looks as if the virus were essential, too.

EDITORIALS

Building Stronger Human Beings

The mental and physical health of a nation depends upon nutrition and that goes back to the soil. Phosphate and lime are the key minerals concerned. The nutrition of about half the people on the earth is inadequate to maintain the 6 per cent of minerals of which the human body is composed. It is the children, principally, who are not being properly fed, and they are the foundation of the state.

B. F. Williamson, writing in the October, 1949 *Scientific Monthly*, pleads for greater improvement and enrichment of the soil; there is not enough research on the naturally occurring legumes and their nitrogen-fixing organisms. Williamson believes that the sea will prove a great and cheap source of needed minerals, the supply of which is threatened, just as we went to the ocean for bromine to produce tetraethyl lead and for magnesium in airplane production.

"Up to the time," says Williamson, "of World War II Germany was getting nearly one third of the phosphate produced in Florida. When I read reports from other states—Ohio, Michigan, Wisconsin, and nearly all the others—they show deficiencies in food. We are shipping billions of pounds of food to Europe—which is fine, but we are also shipping soil fertility, and rapidly approaching a period when our entire population may be on a marginal ration." There is a great deal of talk about this, but little is being done."

The British Nightmare

The organ of the Milwaukee County Medical Society for September, 1949, carries an interesting address by Cecil Palmer, British author, journalist and publisher, before the fifth annual conference of Presidents and Other Officers of State Medical Associations. It is a scathing characterization of British medicine under nationalization, which Mr. Palmer describes as "a contribution to the servile state not exceeded by any previous measure of the sort in any country." It is a system exemplifying perfectly the "curse of state paternalism." The cost of the medical program is only one-ninth of the total bill for social services and Mr. Palmer sees Britain in a financially hopeless condition at the end of another year. Medicine "can not possibly recover." It is a case of "political insanity," one result of which is that "the moral and scientific degradation of medicine is terrible."

The high cost of the program has compelled the Government to reduce the number of hospital beds (and other services), so that many thousands of cases requiring institutional care can not be hospitalized; even if the beds were to be had, there would not be enough doctors and nurses to service them.

The doctor himself is a "glorified clerk," making his case reports in triplicate for the Local Lay Councils and Regional Boards, and getting paid quarterly at the rate of $3.25 per patient per annum. But he pays a 45 per cent direct income tax. His principal obligations and responsibilities are to his new master, the state, which has commandeered him body and soul.

This British witness warns us to be "aware of what may happen to your noble profession if you ever find yourselves under the state."

Only in Union Is There Strength

The reason why the British Labor Government defeated the doctors in their fight for freedom was because it succeeded in splitting the general practitioners and specialists. The Government took advantage

of the specialists' belief that the fight concerned only, or at least chiefly, the general practitioners. It is true that they awakened finally to their own peril and joined the battle, but this move on their part came too late.

American resistance to statism must be solid, collective, total. The British lesson is plain.

Consider the plight of the British specialists now, with even their hospital beds due to be vastly reduced in 1950. The beds are too costly. Who can say that with an inadequate number of beds British medicine will not be lowered in quality?

The improving status of the general practitioner in this country encourages faith in the doctrine that the interest of each member of the American profession is the interest of all. With the goal of medical democracy achieved the politicians will be unable to ensnare us in their social security (so-called) trap. Freedom versus alleged security (on a mediocre level) is the issue.

One great evil in some localities making against a solidly welded profession has been that phase of the closed shop characterized by the taking in, on the part of the specialists who make up such an inordinate part of our hospital staffs, of one another's washing. We mean that the large number of men on many hospital staffs are not much interested, and often not at all, in the referral of patients to them by general practitioners in their communities. A given specialist refers cases out of his line to fellow members of his hospital staff. This system works both intramurally and extramurally. Here is an economic and cultural gap of vast dimensions. How can a profession, so split, form a powerful barrier against federalization? Such a set-up facilitates enormously the machinations of the promoters of the Welfare State (not the same thing as a state of welfare!)

The freezing out of the general practitioner by hospital staffs has gone to extreme lengths. No consideration or courtesy has been shown to him, let alone privileges or honor. Often he could just as well not exist, so far as hospital groups are concerned. His patient in a nearby hospital might just as well be in Alcatraz, so far as access to the sick man or his records is concerned. His status is not as good as that of a pushcart peddler visiting his sick bambino—an unbelievable stupidity as well as foul play on the part of a supposedly civilized profession.

From the crudity of [some of] the medical powers that be
Good Lord deliver us!

Unless the profession cleans up such a sorry mess completely it will *deserve* regimentation by the State. It now definitely invites it. In so far as it is derelict in this respect it is weak in the face of a dire threat to its freedom.

We urge again, as we have for many years, that general practitioners in good standing but unattached to particular staffs receive invitations and reports from hospitals concerning their patients, and have access to records, after being meticulously posted as the referring doctors. Such privileges would not be abused and in themselves have nothing to do with appointments; they have mostly to do with intelligent understanding and care after dismissal and referral back to the practitioner. Such practitioners should at the least be "members of the congregation" if they can not be deacons and priests. It is a simple matter of postgraduate education, administrative diligence, etiquette and decency which should be perspicuous to all but louts. The ensuing good feeling and sense of "belonging" on the part of those recognized would be a fine outcome and well trained younger men would not be so loath to enter the ranks of needed general practitioners.

Benjamin Franklin's terse adjuration to his colleagues before the American Revolution to hang together or else hang separately seems apropos.

The proper relation of the hospital to the general practitioner should be that of a postgraduate community center feeling an educational responsibility for a cooperating clientele and intensively cultivating integration. It should be as accessible to the practitioner and as much a part of himself as the temple of his religious faith.

CONTEMPORARY PROGRESS

PEDIATRICS

A Poliomyelitis Epidemic

F. H. Clark and associates (*Archives of Pediatrics*, 65:496, Sept. 1948) describe an epidemic of poliomyelitis occurring in the city of Jamestown, N. Y., and surrounding area in the summer and early fall of 1947 reaching its peak between September 7 and 20th. There were 46 cases, or 62 per cent, among persons under fifteen years of age, and 28, or 38 per cent, among persons fifteen years of age and over; there were 9 cases in the five-year-old group, and 8 cases in the one-to-four age group. Sixty-four cases were of the spinal type, 4 of the bulbar type and 6 of the bulbospinal type; there were 3 deaths, all in the bulbospinal type. Twenty patients had their tonsils removed; in one case in which tonsillectomy was done one month before the onset of polio, the patient was hospitalized for six months, but shows only mild weakness of one leg. All the patients who developed severe paralysis, with the exception of a boy five years old, had exercised after the onset of the prodromal symptons; one patient, fifteen years of age, who died of the disease, had gone swimming when suffering from muscle pains and headache. This indicates the need of rest during the preparalytic stage. During a polio epidemic, there is naturally much apprehension among parents and children; ordinary disorders may be mistaken for prodromal symptoms of polio. The most frequent early symptoms in cases in which the diagnosis of polio was subsequently established were headache, fever, stiff neck, leg pains, fatigue and backache. But similar symptoms were reported during the epidemic in cases in which the diagnosis of poliomyelitis could not be established; most of these cases were upper respiratory tract infections or "rheumatic manifestations." During the polio season, or during a polio epidemic, persons who show such symptoms should be put to bed until the diagnosis can be definitely established. The signs most frequently found on the initial examination of patients with poliomyelitis were: stiff neck, difficulty in forward flexion (due to spasm of lumbar muscles), and a positive Kernig sign. Spinal puncture was done in most cases; no correlation was found between the spinal fluid cell count and the severity of the disease, but there was a definite correlation between the total protein of the spinal fluid and the severity of the disease. Treatment was by hot packs until the muscle spasm and tightness disappeared; then by passive exercises, followed by assistive and resistive exercise, and muscle reeducation of paralyzed muscles. When a Hubbard tank was installed all patients were treated daily in this tank. In May 1948, 53 patients, or 71 per cent, were listed as completely recovered, and 2 other patients who had had the bulbar type of the disease had also completely recovered except for slightly nasal speech. Eleven patients had moderate weakness or paralysis or involvement of only one extremity; 5 patients, or 7 per cent, had severe paralysis in two or more extremities.

Comment

Most reports of polio epidemics are based on observations made in hospital cases. The simplest explanation of your commentator after a study of many epidemics of poliomyelitis dating back to 1916 is that we often forget that when there is polio in any given community there is also an epidemic of an unclassified throat infection which attacks

hundreds of children who have no manifestation of disease of the nervous system. During such epidemics it is perfectly possible that all these children have an infection with the polio virus. Unfortunately the throat symptoms have disappeared by the time the nervous system has been attacked. The greater the number of polio cases diagnosed in any given epidemic it has often been noted that there was a much more extensive epidemic of throat infections in that community. Also it has often been noted that the more severe the epidemic of throat infection the greater number of polio cases are diagnosed. In other words we do not diagnose polio until it becomes a complication of the pre-existing throat infection. A simple analogy might be in the case of scarlet fever if we did not make a diagnosis of scarlet fever until a complication such as nephritis appeared. Some years ago your commentator encountered an epidemic of fever, headache and vomiting in a group of 20 girls at a girl scout camp. Two of these died of poliomyelitis. It is almost certain that the other 18, all in the same group and showing no involvement of the nervous system, all had the virus of poliomyelitis.

The lesson to be learned is that all children who have an infection of the throat or upper respiratory tract should be treated with penicillin and sulfa drugs in combination and now that we have aureomycin, which we know does attack certain virus infections, why not use this late addition to our medical armamentarium in the hope that it may eliminate the polio virus before it attacks the nervous system. ***H.E.U.***

Streptomycin Therapy for Pertussis

V. H. Gordon and P. J. Almaden (*Journal of Pediatrics,* 34:279, March 1949) report the use of streptomycin in the treatment of 27 cases of severe whooping cough in infants and young children; 28 cases of whooping cough of the same degree of severity and of the same age group treated in the hospital previously were used as controls. The total daily dose of streptomycin employed was 25 mg. per pound of body weight; it was given in equal doses at three hour intervals; in most cases treatment was continued for three to four days after the temperature became normal. No unfavorable reactions to streptomycin were noted. In the majority of the streptomycin-treated patients some improvement was noted within forty-eight hours and definite improvement in three to four days. No significant difference was found between the treated and the control group, in the number of days of hospitalization required, but the hospitalization period was somewhat reduced (by a day or two) in the streptomycin-treated group. The majority of patients in both the treated and the control group were under eight months of age, an age period when the mortality from whooping cough is high; 14 cases in the treated group and 17 in the control group were complicated by pneumonia. The case fatality rate in the control group was 39.3 per cent, but in the streptomycin-treated group it was 7.4 per cent. This reduction in mortality was the most notable effect of streptomycin therapy in severe pertussis in infants and young children. On the basis of these results the authors advise the use of streptomycin in conjunction with hyperimmune serum in all "critically ill hospitalized pertussis patients."

COMMENT

The use of streptomycin seems justified in the treatment of such severely ill children with pertussis. The expense of such treatment must not be forgotten and it must also be remembered that the majority of these children had pertussis complicated by pneumonitis. It might seem advisable to treat such children with penicillin and the sulfa drugs in conjunction. The streptomycin might control the infecting organism of pertussis but penicillin and the sulfa drugs should have a greater effect upon the complicating organisms.

If prophylactic inoculations against pertussis were more universally employed many of the severe cases of pertussis and complications would be eliminated entirely, particularly in children under five year of age. H.E.U.

Homologous Serum Hepatitis in Infants and Children

R. E. Miloshok and associates *(Pediatrics,* 3:651, May 1949) report that 8 cases of homologous serum hepatitis in 7 infants and one child two and a half years of age were seen within the past two years. Five of the infants died with acute hepatic degeneration. Four of these deaths occurred within a three week period; the first 3 had been transfused with reconstituted dried plasma distributed from military sources; the fourth patient was an infant given a replacement transfusion for erythroblastosis fetalis from a professional donor who had never had symptoms of hepatitis and had served as a blood donor before and after this transfusion without complications; it was possible in this case that the virus had been transmitted through contaminated equipment. Since these 4 patients had received their blood or plasma transfusions between January 31 and February 28, 1947, an attempt was made to follow up other infants who had been given plasma in this period. Only 9 of 20 infants could be traced, and of these 9, 7 were in good health, one had been jaundiced and was treated in another hospital for hepatitis with recovery; one developed hepatomegaly without jaundice; these 2 cases are reported as cases 5 and 6 of this series, the latter as hepatitis without jaundice. The 7th case had been seen in the hospital during the preceding year and had died with clinical symptoms of serum hepatitis and acute liver degeneration. The 8th patient was seen early in 1948, and is recovering slowly from hepatitis. In both these cases, the hepatitis developed after blood transfusion. The high mortality in this series of cases is at variance with published statistics, but the fatal cases of serum hepatitis reported in these infants indicate that the prognosis is worse in infancy. The symptoms of serum hepatitis in infants are much the same as those observed in adults. Hepatomegaly was seen in all the cases in the series; a rapid decrease in the size of the liver was always associated with a deterioration in the patient's condition and was "an ominous sign" in the 5 fatal cases.

COMMENT

This study reveals what we are rapidly beginning to appreciate, namely, that every child who is to receive homologous serum should be watched for manifestations of jaundice and that many transfusions are given unnecessarily. With the increasing use of serum globulin for the prevention or modification of measles we might expect to find an increasing number of cases with homologous serum jaundice. So far this increase has not been definitely noted by those who have used the serum globulin in large numbers of children. H.E.U.

Methemoglobinemia: A Cause of Cyanosis in Infants and Children

G. W. Walliker and E. H. Baxter *(Archives of Pediatrics,* 66:143 1949) report 5 cases of methemoglobinemia in children; 4 of these children were infants, thirteen days to two months of age; one was a boy two and a half years of age. The cause of the methemoglobinemia was poisoning by potassium chlorate (used in the treatment of stomatitis) in one case; nitrates in well water used in preparing the food formula in 2 cases; sepsis, and accidental ingestion of sodium nitrite tablets in one case each. The chief symptom of methemoglobinemia in infants and children is extreme cyanosis, which is not relieved by oxygen. This failure of cyanosis in children to respond to oxygen should suggest the diagnosis of methemoglobinemia, which is confirmed by the characteristic chocolate color of the blood;

spectroscopic examination of the blood showing the presence of an absorption band in the red region that is dissipated by the addition of cyanide or alkali; or spectrophotometric determination of the amount of methemoglobin present. The treatment indicated is the intravenous administration of methylene blue in an aqueous solution. The usual dosage employed is 1.5 to 3.0 mg. per kilogram of body weight. In some of the cases reported in literature this treatment has resulted in a rapid disappearance of the cyanosis, within an hour, but in the authors' experience, the conversion of methemoglobin to hemoglobin required several hours. In their later cases, they found it advantageous to supplement the intravenous administration of methylene blue by oral administration of the drug in doses of 10 mg. every four to six hours. Ascorbic acid has been found to be of value in the treatment of idiopathic familial methemoglobinemia and it might be useful as a prophylactic measure to prevent the formation of methemoglobin by those drugs that are known to produce this pigment. It is not indicated as an emergency measure in acute methemoglbinemia due to poisoning or sepsis, as in the cases reported. In the 5 cases reported, all but one of the patients recovered promptly under treatment with methylene blue. One child died; in this case the methemoglobinemia was complicated by severe hemolytic anemia; and whole blood, as well as methylene blue, was given without avail.

COMMENT

This is an interesting report of an unusual series of cases not customarily seen in routine pediatric practice but such information can well be stored away for future reference when such cases are encountered. H.E.U.

Vitamin B_{12} Therapy in Megaloblastic Anemia in Infancy

A. Z. McPherson and associates (*Journal of Pediatrics*, 34:529, May 1949) report the use of vitamin B_{12} in the treatment of megaloblastic anemia of infancy. This type of anemia in infants is comparable to nutritional macrocytic anemia in adults or the macrocytic anemia of sprue or idiopathic steatorrhea, rather than to pernicious anemia. In both the cases reported by the authors there was a history of feeding difficulties; in both the diagnosis of megaloblastic anemia was made by examination of the bone marrow. In one case, a Negro infant, a single injection of 0.002 mg. of vitamin B_{12} produced an immediate reticulocyte response, followed by rapid regeneration of the blood without further therapy. In the second case, a longer course of treatment was required; 0.002 mg. of vitamin B_{12} was given daily until a satisfactory reticulocyte response was obtained. The variable response of the anemia makes it difficult to compare the relative effectiveness of different therapeutic compounds. It is of interest that vitamin B_{12} is effective at all in this type of anemia in infants; there is no definite evidence to show that it is more effective than pteroylglutamic acid in megaloblastic anemia of infants, although it has been found more effective in pernicious anemia.

Amino Acid Tolerance Tests in Children

H. Anfanger and R. M. Heavenrich (*American Journal of Diseases of Children*, 77:425, April 1949) report a study of the effect of the oral administration of gelatin, protein hydrolysate, aminoacetic acid (glycine) and a combination of gelatin and aminoacetic acid on the blood amino nitrogen levels in 24 infants and children, ranging in age from five months to six years. Five of these children had pancreatic fibrosis, one had pancreatic achylia and 6 the celiac syndrome; the others were convalescing from various acute illnesses. It was found that gelatin produced "a good rise" in the amino nitrogen level of the blood in all cases except cystic fibrosis of the pancreas and pancreatic achylia, in which the amino nitrogen curve was flat. Protein hydrolysate produced a rise in amino nitrogen blood levels in all cases, but as it was difficult to administer and caused nausea and vomiting, its use was discontinued. Aminoacetic acid produced a good rise in the amino nitrogen blood levels in all cases; it was easily administered and caused no untoward reaction, and

therefore proved to be "an ideal substance" for demonstrating amino acid absorption and differentiating cystic fibrosis of the pancreas from the celiac syndrome. When a mixture of gelatin and aminoacetic acid was given, the curves for amino nitrogen blood levels were such that this differentiation could not be made.

COMMENT

This is further knowledge concerning pancreatic fibrosis and its differentiation from celiac disease. In the past children who died of what we knew as celiac disease probably had pancreatic fibrosis. Now we have the amino acid tolerance tests and they should be employed in the investigation of all children in the first two or three years of life suffering from chronic intestinal indigestion. ***H.E.U.***

Growth of the Heart Related to Bodily Growth During Childhood and Adolescence

M. M. Maresh *(Pediatrics,* 2:382, Oct. 1948) reports the findings in a series of roentgenograms of the chest made at frequent intervals over a number of years; 3205 roentgenograms were made of 128 patients. The transverse, long and broad diameters of the heart and the internal diameter of the chest were measured in each roentgenogram. It was found that variations in size and shape of the heart were very common in childhood. But in spite of variations in growth curves of the cardiac diameters, there was in general a correlation between the increase in cardiac diameter and an increase in body weight and height in childhood and adolescence. In periods of rapid growth such as often occur in adolescents, there was also fairly rapid increase in the cardiac diameters. These findings indicate that changing cardiac size is "a part of the growth process," rather than an isolated physiologic process. Differences in the transverse diameter of the heart were demonstrated for three groups classified as overweight, medium-weight and underweight. The mean values for cardiac transverse diameter were greatest for the overweight group, least for the underweight group, and intermediate for the medium-weight group, indicating that body build is a factor in determining cardiac size in children as well as in adolescents and adults. Cardio-thoracic ratios do not become progressively greater with advancing age, since the width of the chest increases in children and adolescents in much the same manner as the transverse diameter of the heart. There is, however, considerable variation in cardio-thoracic ratios in normal persons; if this normal variation is recognized, the cardio-thoracic ratio is as satisfactory as any other measurement for evaluating the heart size of any individual from a single roentgenogram. The findings in routine roentgenograms of the chest must be related in each instance to "the basic process of growth and maturation of the individual."

Experimental Use of Testosterone Compounds in Premature Infants

E. K. Shelton and I. S. Mark *(California Medicine,* 69:339, Nov. 1948) report the administration of testosterone to 74 premature infants weighing under 2000 Gm. at birth. In all cases the treatment was begun at twelve hours after birth and continued for three weeks. Some of the infants were given methyl testosterone by mouth, 5 mg. daily, others, testosterone propionate by intramuscular injection, 4 mg. daily. In all the treated infants, the time required to regain birth weight and to gain weight to 2500 Gm. was definitely reduced as compared to untreated controls. In 4 sets of twins, testosterone was given to the smaller infant, while the larger infant was used as the untreated control; in all these cases the smaller treated infant showed a better gain in weight and in somatic development than the untreated twin. No ill effects of testosterone were observed, either during treatment or in follow-up studies throughout the first year. Roentgenograms of the long bones were taken at the beginning of the series and again at the end of the year; no difference in bone age between the treated and the untreated infants was demonstrated, but in general, the infants in both groups showed the slight delay in osseous development that is characteristic of prematures.

OTOLOGY

Histopathological Investigations on the Localization, Number, Activity and Extent of Otosclerotic Foci

Bengt Nylan (*Journal of Laryngology and Otology*, 63:321, June 1949) reports a study of the pathological changes in 121 temporal bones from 74 cases of typical otosclerosis, and an additional 3 cases with pathological bone changes of the "Umbau" type. One of the 74 cases with typical otosclerotic changes was found in a closer study of 50 unselected cases of acute and chronic otitis media; a case of the Umbau type was also found in this group. Of the 74 cases of otosclerosis, 34 were females and 40 males. In 90 per cent of all cases the otosclerotic process in the bony capsule involved the region of the oval window, 50 per cent being associated with staples ankylosis; the round window region was involved in 40 per cent, the cochlear capsule in 35 per cent, the internal auditory canal region in 30 per cent and the semicircular canal capsule in 15 per cent. The otosclerotic process was limited to one region in the capsule in 55 per cent of all the specimens; the stapedial region alone was involved in 40 per cent of all cases, the round window in 8 per cent; a single focus at any other site was rare (7 per cent altogether). The foci were active in 20 per cent of the specimens, quiescent in 30 per cent and mixed in 50 per cent; if several foci were present in a single temporal bone, they were usually of the same degree of activity. The extent of the otosclerotic process varied from 0.4 mm. to more than 20 mm., but no correlation was demonstrable between the extent, the localization and the activity of the foci. Pathological changes of the Umbau type were found in a number of the specimens with typical otosclerotic changes, but these Umbau changes were localized chiefly in the semicircular canal and rarely in the cochlear capsule and the vestibule, a localization differing so definitely from that of the otosclerotic changes that the author does not accept the hypothesis that the Umbau is a primary stage of otosclerosis. Further study is required to determine the exact nature of the so-called Umbau type of pathological bone change and its relationship to otosclerosis.

COMMENT

This report is a very useful addition to the mass of factual material which is being accumulated in the study of otosclerosis. L.C.McH.

Acoustic Function Before and After Operation for Otosclerosis

H. Evertsen (*Archives of Otolaryngology*, 49:393, April 1949) reports that the fenestration operation has been performed in 85 cases of otosclerosis at the Sundby Hospital, Copenhagen; 69 of these patients have been kept under observation for one to thirteen months since the operation. Speech tests in these cases showed slight deterioration of hearing for speech in 2 cases, no change in 11 cases, slight improvement in 16 cases, and definite improvement in 40 cases, or 58 per cent. In the group in which the hearing distance for speech was less than 10 cm. prior to operation, definite improvement resulted from the operation in only 18 per cent, indicating that this group is not suitable for the fenestration operation. If this group is excluded, the fenestration operation resulted in definite improvement in hearing for speech in 19 of 26 cases, or 77 per cent. Of 41 patients operated on more than six months ago, 30 are still under observation. The speech tests show that in 19, or 63 per cent, hearing for speech is definitely improved. In the least fit group (hearing distance for speech less than 10 cm.), definite improvement is shown in 15 of 20 patients, i.e., 75 per cent. Audiometer tests in these 30 patients showed definite improvement in hearing in 18 patients or 60 per cent. This shows that results obtained with the speech test are in close agreement with the audiometer tests. The Rinne test was repeated after operation in 19 of the 69 patients under observation; in 12 of these bone conduc-

tion was better than air conduction and in these cases the bone conduction as well as the air conduction at this frequency had been prolonged by the operation; in 7 cases the air conduction was better than the bone conduction.

COMMENT

Figures as given in this summary are a little confusing and the author uses a little different method of studying the patients than those who have been reporting upon results of fenestration operations in this country. However, there is not as yet standardization in methods of reporting results even among the group who are doing this surgery in the United States. ***L.C.McH.***

Radiation Therapy for Conductive Deafness

H. C. Rosenberger (*Archives of Otolaryngology*, 48:504, May 1949) reports the use of irradiation of the nasopharynx for the treatment of conductive deafness in 21 children two and a half to fourteen years of age. In each case, tonsils and adenoids had been removed previously. Selection of patients for this treatment was based on the history, the otologic examination, examination of the nasopharynx and the hearing tests. The typical history in these cases was of recurring colds, frequently associated with varying combinations of otalgia, stuffiness of the ears, tinnitus and variable hearing. The tympanic membranes were usually pink and retracted, but occasionally were lusterless and thickened. Only rarely did the nasopharyngoscopic examination show definite evidence of obstructing lymphoid tissues. In children it is often difficult to visualize the nasopharynx adequately to ascertain the location of obstructing lymphoid tissue; such obstructing lymphoid tissue may be within the lumen of the cartilaginous portion of the eustachian tube or posterior to the torus tubarius. The author has employed roentgen irradiation of the nasopharynx, rather than radium, in the treatment of conductive deafness, because a larger field can be safely irradiated and the lymphoid tissue exposed to the therapeutic rays, whatever its location. In the series reported, the factors employed were 200 kv., 0.5 mm. copper filtration at 50 cm. target skin distance; four treatments were given in each case. Postirradiation hearing tests made several weeks after the last treatment showed 7 patients, or one-third of the series, had a significant improvement of hearing, in some cases a gain of as much as 30 decibels in the critical frequencies. Other forms of treatment employed previous to irradiation therapy had been of no benefit. It is possible that if more than four treatments had been given the percentage of favorable results would be increased.

COMMENT

It is well known that radiation therapy, either by x-ray or radium, causes shrinkage of lymphoid tissue in the nasopharynx as well as elsewhere. We are extremely skeptical that this therapy is of any value for deafness except in instances where lymphoid tissue is causing or contributing to a conductive deafness. ***L.C.McH.***

Modified Radical Mastoidectomy

S. H. Baron (*Archives of Otolaryngology*, 49:280, March 1949) reports 10 cases in which a modified radical mastoidectomy was done for chronic suppurative otitis media. In the first 7 cases the postauricular route was employed, in the last 3 cases, the andaural route; the author now employs the endaural route for both radical and modified radical mastoidectomies. In one of the 10 cases the modified Lempert incision was used. Cholesteatoma was present in 8 of the 10 cases, and in each case the matrix was left in situ. A dry ear was obtained by the operation in all of the 10 cases. In 5 cases, hearing was improved 10 or more decibels for frequencies 512, 1024 and 2048 cycles per second; in 2 cases hearing for these frequencies was improved 7 decibels; in one case hearing for these frequencies was reduced 5 decibels; in 2 cases the hearing charts were not available for this report. During the period when these 10 modified radical mastoidectomies were done, there was one case of chronic suppurative otitis media in which a radical mastoidectomy was performed. From his own experience and from a review of the literature, the author concludes that the

modified radical mastoidectomy is "the ideal operation" in certain cases of chronic suppurative otitis media, and "should supplant the radical operation more often than it does." The modified radical operation preserves the hearing better than the radical mastoidectomy and gives a dry ear as often (or perhaps more often) than the radical operation.

COMMENT

It is well to call our attention to this operation because certainly many patients get excellent results from modified radical mastoidectomy. The selection of cases requires careful study. ***L.C.McH.***

Experiences of Penicillin Treatment in Acute Otitis Media

N. Grebelius and A. Sjöberg (*Journal of Laryngology and Otology*, 63:286, May 1949) report the treatment of 366 cases of acute otitis media treated with penicillin; 329 cases treated in 1943 before penicillin was available in the same hospital are used as controls. Bacteriological studies in the pencillin treated cases showed that hemolytic streptococci and Staphylococcus aureus predominated and that 91.6 per cent of all the organisms isolated were sensitive to penicillin *in vitro*. Treatment was begun by giving three injections of pencillin daily, in doses of 15,000 to 75,000 units for children under fifteen, according to age, and 100,000 units for adults; in 184 of the 366 cases, however, it was necessary to increase the number of injections daily. Penicillin treatment was begun as soon as the patient was admitted to the hospital, and, in uncomplicated cases, was discontinued two to three days after all discharge had stopped. The average duration of hospitalization in the cases treated with penicillin was 11.9 days; in the control series, the average duration of hospitalization was 20 days for those not treated with sulfa drugs, and 14.6 days for those treated with sulfa drugs. The duration of the discharge from the ear in the cases treated with penicillin was 8 days; in the control series the duration of the discharge was 12.7 days with sulfa treatment and 15.9 days without sulfa treatment. No untoward reactions to penicillin were observed, except that in 2 cases there was a rise in temperature considered to be "drug fever." Mastoidectomy was required in only 9, or 2.6 per cent, of the patients treated with penicillin; in no case was a "masking" effect of penicillin on the symptoms of mastoiditis observed.

COMMENT

The experience recorded at least roughly parallels the experience of otologists and pediatricians in this country in that penicillin as well as the sulfas have greatly reduced the incidence and complications of acute otitis media. ***L.C.McH.***

RHINOLARYNGOLOGY

Postnasal Discharge

B. L. Bryant (*Laryngoscope*, 59:397, April 1949), in his study of patients with extensive postnasal discharge, has found that this symptom is "almost invariably" associated with enlargement of the posterior tips of the inferior turbinates; demonstrable sinus disease may or may not be present. This hypertrophy is not usually visible on casual inspection of the nose, and sometimes cannot be demonstrated by posterior rhinoscopy, but can be visualized by means of the nasopharyngoscope. In other cases, this hypertrophy can be seen readily by anterior rhinoscopy, but because this is not always the case, the use of the nasopharyngoscope is indicated in every routine examination of the nose. It has often been noted that postnasal discharge persists after sinus surgery, but the author has found that this discharge ceases when the posterior tip hypertrophy is adequately treated. He has also found that with adequate treatment of this hypertrophy, the postnasal discharge ceases and the associated sinus condition clears up

without surgery or that other methods of treatment, such as the Proetz displacement therapy, are effective. For eleven years, the author has treated such hypertrophy of the posterior tips of the inferior turbinates by the application of phenol to the hypertrophied area. For this purpose, a thin, light, malleable wire applicator is used, wrapped very tightly with cotton, which is then compressed. The nose is first sprayed with cocaine-hydrochloride (2 per cent). Then a 20 per cent solution of the same drug is applied with the applicator to the turbinate tips for ten minutes. For the application of the phenol, the amount of cotton at the end of the applicator is very small; the applicator is introduced parallel with the floor of the nose and turned laterally to reach the posterior tip of the turbinate at the proper depth, so that the phenol is applied precisely to the hypertrophied area. Treatments are repeated at intervals of at least a week until nasopharyngoscopic examination shows that the hypertrophy is entirely eradicated, even though symptoms have been entirely relieved earlier. A study of biopsy specimens from the posterior tips after a series of phenol treatments has shown that the ciliated epithelium returns to normal.

COMMENT

Chemical cauterization of hypertrophied lower turbinates has been used for many years. Most rhinologists prefer submucous electrocoagulation or the injection of sclerosing solutions or sometimes even removal of such hypertrophied turbinal tips. We are inclined to feel that they are more often secondary to sinus infection rather than being the cause of sinus infection. L.C.McH.

Penicillin Aerosol Therapy in Sinusitis

F. J. Hynes (*Annals of Otology, Rhinology and Laryngology*, 58:189, March 1949) reports the treatment of 212 cases of sinusitis, 104 of which had been previously reported, with penicillin aerosol with oxygen, using the apparatus of Barach. Treatments with 40,000 units of penicillin were given daily. Other treatment consisted only in making sure that the sinus openings were "clear and available;" this was done by shrinkage and occasionally by suction irrigation. In the entire series of 212 cases, results of the penicillin aerosol therapy were classed as clinical cures in 50 cases, marked improvement in 34 cases, moderate improvement in 45 cases, slight improvement in 19 cases and no improvement in 34 cases. The average number of treatments in these 212 cases was 10.6; in the original group of 104 cases, the average number of treatments was 12. Of these 104 patients, 67 returned for recheck and 17 of these showed improvement in the x-ray findings; one of these patients had not completed treatment as advised, having had only eight treatments. In the treatment of acute upper respiratory infections with involvement of the nasal sinuses, the author considers that penicillin aerosol therapy with oxygen is the treatment of choice. If pus is present, however, it must be drained. Good results are often obtained in acute exacerbations of chronic sinusitis, and occasionally "spectacular" results are obtained in chronic sinusitis; in these chronic cases, the author believes the results are to be attributed to the oxygen rather than to the penicillin.

COMMENT

We are inclined to suspect that this type of therapy is enjoying popularity at the present time which will probably wane during the next few years. L.C.McH.

Streptomycin Treatment of Ozena

K. M. Simonton (*Proceedings of the Staff Meetings of the Mayo Clinic*, 24:337, June 8, 1949) reports the treatment of 8 cases of ozena with streptomycin; 5 of these cases were treated in 1945 and 3 in 1946. In all these cases, cultures of material from the nose were positive for Klebsiella organisms. In the more advanced cases of ozena the Klebsiella organisms are regularly found in cultures from the nose; but in children suspected of having the initial phase of ozena cultures have not uniformly showed these organisms, suggesting that Klebsiella is a secondary invader in cases of ozena. The daily dosage of streptomycin employed in the 8 cases treated varied from 800,000

units to 2,000,000 units, given in divided doses for five to fourteen days; the last 3 patients treated received 2,000,000 units daily seven to fourteen days. Symptomatic improvement occurred at the time of treatment in 7 of the 8 patients; but the atrophy of the nasal mucosa was not affected. While none of these patients have returned to the Clinic for observation, 7 have reported by letter eight or more months after treatment; of these 5 reported definite relief of symptoms, such as diminution or complete disappearance of suppuration, crusts and odor. Suppurative sinusitis of long duration was present in 2 patients; in one of these with chronic suppuration of the right antrum, a nasoantral window was made at the time of streptomycin therapy; this patient has shown definite improvement and reports disappearance of crust formation and suppuration. In the other case repeated sinus operations had been done, but the sinuses were draining pus at the time of streptomycin therapy; this patient showed no improvement. Recently 3 patients with ozena have been treated with streptomycin in a dosage of 1 Gm. daily by intramuscular injection, and 0.5 to 1 mg. daily by nebulization; the immediate response to treatment was favorable. The results justify further trial of streptomycin therapy in ozena; the effect of antibiotic therapy in early cases of ozena, before atrophy of the mucosa has occurred, should also be studied.

COMMENT

Until now the most effective therapy of ozena has been to train the patient literally to keep his nose clean. Streptomycin is certainly worth a trial in these patients. We suspect that recognition of ozena before atrophy of the mucous membrane has occurred would be very difficult. ***L.C.McH.***

Scleroma of the Larynx, Trachea and Bronchi

A. H. Miller *(Laryngoscope,* 59:506, May 1949) reports 3 cases of scleroma of the larynx, trachea and bronchi. In these cases, and in others observed by the author, the typical lesion, obstructing granulomatous infiltration, involved the larynx subglotically; the true cords, however, may show slight reddened infiltration with restriction of movement. The lesions in the trachea and bronchi were of the diffuse concentric-infiltrative type in either the granulomatous stage or the later fibrotic stenotic stage. Any stenotic obstructing lesion of trachea and bronchi with laryngeal involvement should be suspected of being scleroma. If biopsies are difficult to obtain or do not show all the characteristics of the disease, diagnosis may be made by biopsies from nasal lesions; diagnosis of scleroma was established in this way in the 3 cases reported; Klebsiella organisms were isolated in all cases. In these cases, treatment with streptomycin gave good results; streptomycin was given by intramuscular injection (1 Gm. daily in divided doses) and also by nebulizer (½ Gm. daily). All these patients were Mexicans living in southern California and were admitted to the Los Angeles County Hospital. Although at one time it was thought that scleroma of the respiratory tract occurred only in the Balkan states, it is now recognized that it may occur anywhere; the first case recognized in California was reported in 1914.

COMMENT

These are interesting case reports and streptomycin therapy seems to be very hopeful ***L.C.McH.***

Carcinoma of the Nasopharynx: Report of 150 Cases

M. W. Simmons and I. H. Ariel *(Surgery, Gynecology and Obstetrics,* 88:763, June 1949) report 150 cases of carcinoma of the nasopharynx from the Hines Veterans Administration Hospital. All these patients were males; the average age was forty-five years; 32 patients (21.3 per cent) were below forty years of age. The need for considering the possibility of cancer of the nasopharynx in the younger age groups is emphasized. The most common site of origin of the growth was Rosenmueller's fossa. In these cases swelling of the neck was the most common initial symptom; pain on the side of the

face and head was the next most common symptom; the initial symptoms were rarely referable to the nasopharynx. Symptoms of cranial nerve involvement, most frequently the sixth nerve, were present on admission to the hospital in 44 patients (22.3 per cent) and cranial nerve paralysis occurred at some time during the course of the disease in 55 patients (36.6 per cent). Careful examination of the nasopharynx and biopsy of suspicious areas are indicated in cases of metastatic cervical neoplasms and in cases with cranial nerve symptoms. In all cases in this series the diagnosis was confirmed by biopsy. Treatment of cancer of the nasopharynx is by irradiation, preferably by fractionated x-ray therapy. Supplementary therapy with Martin-Blady nasopharyngeal radium may be indicated. Cervical and other metastases are also treated by radiation. Of 78 patients observed five years and more ago, 7 are living, making the five-year survival rate, 9.8 per cent. In 7 patients who were not treated, the average period of survival was seventeen months; adequate x-ray therapy increased the average duration of life to thirty-one months; in a few cases in which only palliative radiation to either the metastases or to the primary lesion alone was employed, this did not significantly increase the duration of life, but did give marked relief of symptoms. On an average, in this series, 10.1 months elapsed after the occurrence of a significant symptom before adequate therapy was given.

COMMENT

Carcinoma in this region is almost always recognized late and the results of therapy are quite discouraging. ***L.C.McH.***

OPHTHALMOLOGY

The Lability Test: A New Procedure for the Diagnosis of Chronic Simple Glaucoma

S. Bloomfield (*New York State Journal of Medicine*, 49:659, March 15, 1949) describes a new test for chronic simple glaucoma, which has been found to be of definite aid in the early diagnosis of this condition before irreversible injury has been done to the eye. Patients with chronic simple glaucoma in the early stage may have ocular tensions within the normal range, even on repeated examinations, and while the symptoms may be suggestive of glaucoma, the functional and anatomic signs may not be sufficient for a definite diagnosis. In such cases the lability test described has been found of value. The tension of each eye is first determined. The patient then places one hand, open, up to the wrist in ice water; and at the same time a blood presure cuff, previously placed loosely around the neck, is inflated to a pressure of 50 to 60 mm. of mercury. At the end of one minute, the ocular tension is again recorded, while the patient's hand is still in ice water, and cervical pressure is maintained. In this test, the water must be ice cold, chipped ice or ice cubes usually being placed in the water fifteen minutes before the test. The bladder of the pressure cuff must be applied anteriorly on the neck so that both jugular veins are compressed; with the pressure maintained just below 60 mm., the arterial circulation is not impeded, and the patient can breathe quite easily. The use of this test in a large series of cases has shown that a rise in ocular tension of more than 9 mm. of mercury (Schiotz) indicates abnormal lability or intra-ocular tension and suggests the presence of chronic simple glaucoma; also a rise in tension to over the normal limit of 30 mm. of mercury (Schiotz) is more conclusively indicative of chronic simple glaucoma, whether or not the actual rise is more than 9 mm. In one series of tests in cases of chronic simple glaucoma under medical treatment, medication was discontinued under observation. After the effect of medication had worn off, the ocular tension remained within normal limits for twenty-four hours in many instances, but within that period

the lability test produced an abnormal response, indicative of chronic simple glaucoma, in 91 per cent of these cases. The test is simple and can be more rapidly done than other tests used in the diagnosis of chronic simple glaucoma.

Ocular Myasthenia Gravis

J. V. Lisman (*American Journal of Ophthalmology*, 32:563, April 1949) reports 2 cases of ocular myasthenia gravis in which only the eyes were involved. In the first case, the only symptom was diplopia, which had been present for a month; the patient stated that there had been another episode of double vision, fourteen years previously, which had subsided in a few weeks. The diplopia was found to be due to paresis of the left superior oblique muscle; there was no evidence of involvement of any other muscle. On attempting to chart the diplopia field with the aid of a red filter, it was found that the diplopia increased as the examination was continued; this increase of muscular weakness with fatigue was considered indicative of a myasthenic reaction. An injection of prostigmin methylsulfate (1.5 mg.) combined with atropine sulfate (0.6 mg.) relieved the diplopia immediately. The patient was placed on oral therapy with prostigmin with a dosage of three tablets (15 mg.) daily, given in divided doses, so that no diplopia occurred during the day. The patient also noted a feeling of strength and well being. In the second case the first symptom noted was also diplopia; later difficulty in raising the left upper eyelid developed. At the time the patient came under observation, there was almost complete ptosis in both eyes, increased by repeated attempts to raise the eyelids. All movements of both eyes were diminished and the eyeballs could not be rotated beyond 15 degrees from fixation; thus there was almost complete paralysis of all extraocular muscles, as well as inability to rotate the eyes conjugately. When an intramuscular injection of prostigmin methylsulfate (1.5 mg.) and atropine sulfate (0.6 mg.) was given, there was marked improvement in the ptosis and increase in the ocular motility with some increase in the power of the orbicularis oculi; the diplopia still persisted. No evidence of any involvement of any other muscles in the body was found in this case, but the patient stated that he felt stronger after the administration of prostigmin. No maintenance dose of prostigmin was determined as the patient did not remain under observation. As myasthenia gravis may involve the eyes primarily, as in the cases reported, the ophthalmologist should be aware of the various possible manifestations of this disease. The signs of myasthenia gravis may be localized in the eyes for many years, or the ocular manifestations may be followed rapidly by involvement of muscles of the trunk and extremities. It is possible that some cases of so-called "functional" diplopia, transient convergence weakness and mild transitory ptosis are early cases of myasthemia gravis.

Use of Phenylephrine Hydrochloride (Neo-Synephrine Hydrochloride) in Ophthalmology

P. Heath and C. W. Geiter (*Archives of Ophthalmology*, 41:172, Feb. 1949) report a study of the effect of phenylephrine o nthe bloo dpressure and intra-ocular pressure when the drug was instilled into the eye. When given by mouth or parenterally phenylephrine causes a marked rise in blood pressure, but its absorption through the anterior chamber of the eye is slow and limited. In a study on 60 clinic patients and 60 private patients with various ophthalmic and general diseases, including incipient glaucoma, cataract and hypertension, the blood pressure and intra-ocular pressure were determined before and one hour after the instillation of phenylephrine into the eye. No significant change in either blood pressure or intra-ocular pressure was produced, except that in cases with narrowed angle, blockage from iris tissue may occur as the pupil is dilated, with resultant increase in intra-ocular pressure. The authors have never noted any harmful effects of phenylephrine on the ocular tissues or the blood vessels. Phenylephrine hydrochloride has been found to have a wide range of use in ophthalmology.

As a decongestive agent for mild conjunctivitis 0.0125 per cent phenylephrine may be used in association with other drugs. For "substantial" decongestion of the globe a 10 per cent emulsion may be used, or a 10 per cent solution instilled after the use of a topical anesthetic. Phenylephrine hydrochloride is of value as a mydriatic in many conditions, including: examination of the fundus; in breaking adhesions of the iris to the lens; in refraction, especially in cases of presbyopia and myopia; in cycloplegia when the iris is resistant to dilation; in overcoming extreme miosis in glaucoma; in beginning an intra-ocular operation, in which a widely dilated pupil at the time of operation is necessary, but it is desirable to have it contract shortly after operation; in provocative testing for glaucoma induced by dilated pupils; as a supplement to a mydriatic when there is sensitivity to the latter. In glaucoma phenylephrine may be used in conjunction with miotics; its decongestive effect is valuable. If the increased intraocular pressure is based on mechanical blockage at the angle, weak solutions of phenylephrine should be tried until the solution having the most effective action is determined.

Use of Privine-Antistine Drops in Ophthalmology

R. R. Daily and Louis Daily, Jr. (*American Journal of Ophthalmology*, 32:441, March 1949) report the use of Privine-Antistine drops in about 100 cases of conjunctivitis of various types. Privine is chemically a nephthyl-methyl-imidazoline hydrochloride, soluble in water or saline solution. When instilled into the conjunctival sac Privine solution causes a vasoconstriction similar to that produced by adrenalin, but persisting for a longer time and not followed by secondary vasodilatation; it causes slight pupillary dilatation, which is noticeable only in dim light and in eyes with blue irises. It has no significant effect on intra-ocular pressure. Antistine is a synthetic antihistamine drug. In the treatment of conjunctivitis, the authors have employed a combination of 0.5 per cent Antistine and 0.025 per cent Privine. Instillation of this solution into the eye caused a smarting sensation of short duration in most cases followed by definite relief of burning, itching and photophobia. In cases of conjunctival congestion with subjective symptoms such as burning, itching, a feeling of sand in the eyes, fatigue and blurring of vision, but with no evidence of infection, the Privine-Antistine solution has been found to give prompt relief of symptoms. It also gives relief in conjunctival irritation following trauma, burns and chemical injuries. In cases of conjunctivitis with pronounced follicles, Privine-Antistine drops are instilled every four hours. Relief of symptoms results from this treatment, which is superior to that obtained with other medicaments used to give transitory relief in cases of this type. The solution employed may be used indefinitely without causing untoward reactions, so that it is of value in treatment of chronic conjunctivitis. The solution can be combined with astringents in chronic conjunctivitis or with silver preparations in acute conjunctivitis, if indicated. The solution gives some relief of subjective symptoms and reduces bulbar congestion in scleritis and episcleritis, but the therapeutic effect is not as marked as in conjunctivitis. It may be used to advantage with local anesthetics such as pontocaine or holocaine, as it reduces the conjunctival irritation often caused by these anesthetics.

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HEPATITIS

—Concluded from page 517

given as a salt. Inositol may be helpful.

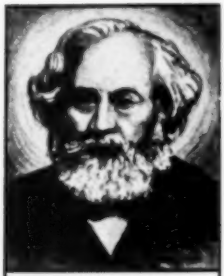
The prognosis in hepatic insufficiency is directly dependent upon the amount of good liver tissue which survives the attack. The avoidance of hepatotoxins is extremely important. Alcohol is contraindicated. Contact with cleaning solutions (CCl_4), benzols, DDT, toxic inhalants, and all oral toxins is to be avoided. The tremendous liver reserve and the ability of the liver to regenerate lead to a favorable outlook in most cases properly managed.

2405 Fourth Avenue.

Medical BOOK NEWS

Edited by
ANDREW M. BABEY, M.D.

All books for review and communications concerning Book News should be addressed to the Editor of this department, 1313 Bedford Avenue, Brooklyn 16, N. Y. When books are sent to us with requests for review, selections for that purpose are promptly made.



SIR SAMUEL WILKS
1824 - 1911

Classical Quotations

● The purport of these remarks is that, in endocarditis or valvular disease of the heart attended by the presence of vegetations or fibrinous coagula, a blood poisoning may occur, giving rise to all the symptoms of pyaemia; and also that these may exist to a lesser degree in the form merely of pyrexia, prostration, pain in the joints.

SIR SAMUEL WILKS

Abstract of a Clinical Lecture on Pyaemia as a Result of Endocarditis. *Brit. M. J.*, *1*:279, 1868.

Refraction

The Practice of Refraction. By Sir Stewart Duke-Elder, M.D. 5th Edition. St. Louis, C. V. Mosby Co., [c. 1949]. 12mo. 317 pages, illustrated. Cloth, $6.25.

This is a very well written and instructive volume of 309 pages including the appendix, with numerous very satisfactory illustrations. It contains numerous revisions.

One of the most valuable sections, which should appear in every work on refraction, deals with the nature and incidence of refractive errors. There is a discussion of the relation of index myopia to axial myopia. Reference is made to Steiger's work, to the norms of refraction by modern writers and to methods of measuring the actual size of the eyeball by means of the X-ray theory.

This small volume is in a sense an abstract of the writer's more celebrated four-volume *Textbook of Ophthalmology*, particularly volumes one and four. It is very valuable for classroom work and for purposes of review.

The only improvement that the reviewer could suggest would be the inclusion of a list of reference works so that the student would be able to elaborate on his studies from authentic sources should he so desire.

JOHN N. EVANS

Business and Medicine

The Business Side of Medical Practice. By Theodore Wiprud. 2nd Edition. Philadelphia, W. B. Saunders Co., [c. 1949]. 12mo. 232 pages, illustrated. Cloth, $3.50.

Most physicians can be said to have only an incomplete conception of the business management of practice, proper records and various legal ramifications connected with their work. This volume cover many practical points such as investments, insurance, wills and estate, court testimony, press relations, conducting a meeting, etc. It can be recommended as most timely.

ANDREW BABEY

Visual Defects

Help Yourself to Better Sight. By Margaret Darst Corbett. New York, Prentice-Hall, [c. 1949]. 12mo. 218 pages, illustrated. Cloth, $2.50.

This work is a resurrection of the theories and methods advised by the late Dr. William H. Bates, in the treatment of visual defects by means of exercises and manipulations. It has no value whatever from a scientific viewpoint and contains many misstatements and much false reasoning.

JOHN N. EVANS

—Continued on following page

MEDICAL BOOK NEWS

—Continued from preceding page

History Taking

Clinical Case-Taking. Guides for the Study of Patients. History-Taking and Physical Examination or Semiology of Disease in the Various Systems. By George R. Herrmann, M.D. 4th Edition. St. Louis, C. V. Mosby Co., [c. 1949]. 8vo. 240 pages. Cloth, $3.50.

This little volume is a fairly complete resumé of what constitutes a good history and full physical examination in medicine, neuropsychiatry, pediatrics, and surgery. It has much useful, fundamental information. It should be referred to often by every practitioner regardless of his specialty.

ANDREW BABEY

Atoms

Constructive Uses of Atomic Energy. Edited by S. C. Rothmann. New York, Harper & Bros., [c. 1949]. 8vo. 258 pages, illustrated. Cloth, $3.00.

The potential value of atomic energy in the war effort is fortunately or unfortunately well known today but the future of atomic energy rests in a myriad of possibilities in commercial and medical pursuits. This book is devoted to that purpose. Peering into the future one meditates, yet enthusiastically awaits, the new vistas so near and yet so far away, that will probably revolutionize our living of the future. In reading the book one needs but elementary knowledge of nuclear fission to obtain an understanding of radiation effects. Gamma and X-radiation, formerly employed by therapists in medicine only, will be better understood and their applicability in the commercial fields better appreciated. From various authorities articles have been extracted, many of which have previously appeared in print, which describe for the average reader the future possibilities of atomic energy in the fields of electric power, metallurgy, chemistry, biology, medicine and soil fertilization.

For an introduction to the subject of atomic energy, its physics and constructive usages, this book is heartily recommended.

MILTON G. WASCH

—Concluded on page 554

emotional equilibrium for the geriatric patient

Thousands of doctors know that BENZEBAR* allays the mental depression, apprehension and nervousness so frequently found in the elderly patient.

'Benzebar' is S.K.F.'s logical combination of Benzedrine* Sulfate and phenobarbital. It provides the unique improvement of mood of 'Benzedrine' Sulfate and the calming, soothing influence of phenobarbital. These two established agents work together to restore the elderly person's zest for life and living, to quiet his nervousness and, at the same time, to keep him from overdoing.

Each 'Benzebar' tablet contains: 'Benzedrine' Sulfate, N.N.R. (racemic amphetamine sulfate, S.K.F.), 5 mg.; phenobarbital, ¼ gr.

Smith, Kline & French Laboratories, Philadelphia

Benzebar for the depressed and nervous patient

*'Benzedrine' and 'Benzebar' T.M. Reg. U.S. Pat. Off.

MEDICAL BOOK NEWS

—Concluded from page 542

Diabetes

Diabetic Menus, Meals and Recipes. By Betty M. West. New York, Doubleday & Co., [c. 1949]. 8vo. 254 pages. Cloth, $2.95.

The author of this volume is a diabetic with no previous technical training in dietetics who found it necessary to acquaint herself with the practical aspects of diabetic menu preparation. She has gathered her experiences into this small volume which is in reality a cook book for diabetics, containing a large list of recipes with their calculated carbohydrate, protein, and fat values.

WILLIAM S. COLLENS

Juvenile Delinquency

Protecting Our Children from Criminal Careers. By John R. Ellingston. New York, Prentice Hall, [c. 1948]. 8vo. 374 pages. Cloth, $5.00.

This book describes the traditional method of treating criminal behavior in children, with its accompanying chaos, cruelty and ineffectiveness. This is followed by a description of the "Youth Authority Act", now established in California, Minnesota, Wisconsin, and Massachusetts, wherein the entire handling of the delinquent youth is turned over to the "Youth Authority."

The book has an appeal for those physicians especially interested in Juvenile Delinquency.

STANLEY S. LAMM

Heart

Clinical Auscultation of the Heart. By Samuel A. Levine, M.D. & W. Proctor Harvey, M.D. Philadelphia, W. B. Saunders Co., [c. 1949]. 8vo. 327 pages, illustrated. Cloth, $6.50.

Levine and Harvey's monograph on *Clinical Auscultation of the Heart* takes its place at once as the definitive work in its field. Every aspect of this clinically important subject is thoroughly covered and there are numerous cardiograms and heart sound tracing. This small volume will be invaluable to the general practitioner and to his cardiologist colleagues.

MILTON PLOTZ

Greater Safety

in Dual Sulfonamide Therapy

Each teaspoonful (5 cc.) of Aldiazol-M provides:

Sulfadiazine (microcrystalline)	0.25 Gm.
Sulfamerazine (microcrystalline)	0.25 Gm.
Sodium Citrate	1.0 Gm.

With Aldiazol-M, adequate sulfonamide dosage may be administered with utmost therapeutic advantage and with minimal danger of crystalluria. Providing both sulfadiazine and sulfamerazine in equal amounts, it permits greater total urinary sulfonamide saturation. Thus the risk of crystal precipitation is reduced, even when large amounts are given.

Because its sulfonamides are in microcrystalline form, Aldiazol-M leads to rapidly attained initial levels. Thereafter therapeutic blood levels are maintained on a dosage of 2 teaspoonfuls every four hours (1 Gm. of total sulfonamide). The presence of sodium citrate in Aldiazol-M makes unnecessary the administration of other alkalizing agents.

Aldiazol-M is indicated in many infectious diseases which respond to sulfadiazine and sulfamerazine. Pleasantly flavored, it is especially useful in pediatric practice.

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SEMCO

ALDIAZOL-M

Modern THERAPEUTICS

Effect Of Aureomycin On Pertussis

Aureomycin was found to produce such favorable results in the treatment of experimental infections of pertussis in mice that clinical trial was begun. In experimental studies on mice the animals were innoculated intracerebrally with a suspension of a culture of *Hemophilus pertussis*. Bell, Pittman and Olson reported that the animals were then treated by the subcutaneous injection of aureomycin in a total amount of 0.078 to 32.0 mg. Other factors were also varied in that frequency of treatment varied from 1 to 4 times a day, the duration of treatment from 1 dose to 8 days of treatment, and the interval between injection of the culture and the beginning of treatment from 6 to 96 hours. The results from these experiments indicated that in general a treatment regime of small doses given at frequent intervals over a period of several days delayed and prevented deaths more effectively than larger doses given singly or at frequent intervals for fewer days.

The authors also reported, in *Pub. Health Rep.* (64:589 (May 13, 1949)) that a preliminary trial in 20 cases of pertussis in children from 1 month to 6 years of age suggested a definite prompt and gradual reduction in the frequency of paroxysms and a shortening of the clinical course of the disease. The best results were obtained in those children in which treatment was started early in the course of the disease. The dosage employed was 0.5 Gm. per Kg. of body weight in divided doses over a period of 8 days. No untoward effects resulted from this treatment.

Chloromycetin In Experimental Cholera Infections

Complete inhibition of *Vibrio comma* was obtained with 0.005 mg. of Chloromycetin per cc. of culture media in *in*

—Continued on page 54a

when MIGRAINE *attacks*

FIRST EFFECTIVE

oral TREATMENT

OF MIGRAINE ATTACK

Sandoz proudly announces the *first effective oral* treatment of migraine—

Clinical investigation[1] demonstrated that 80% of a series of cases experienced good results. Best results were obtained in migraine, histamine and tension headaches.

Friedman,[2] in a large series of migraine cases, found Cafergone 55% more effective than ergotamine tartrate alone.

Later reports[3, 4] were equally favorable.

1. Horton, B.T., Ryan, R. E. & Reynolds, J. L., Proc. Staff Meet. Mayo Clinic, 23:105, Mar. 3, 1948.
2. Friedman, A. P., N. Y. State Jl. of Med. (in press).
3. Ryan, R. E., Postgraduate Medicine (in press).
4. Hansel, F. K., Annals of Allergy (in press).

Cafergone

SANDOZ

(ergotamine tartrate 1 mg.; caffeine 100 mg.)
(Experimentally identified as E.C. 110)

Originality • Elegance • Perfection

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Division of SANDOZ CHEMICAL WORKS, INC.
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MODERN THERAPEUTICS

—Continued from page 52a

vitro experiments. Gauld *et al* also reported the results of experiments in mice in *J. Bact.* (57:349 (Mar. 1949)). Provided adequate doses of Chloromycetin were given within 2 hours following the intraperitoneal inoculation of the mice with the vibrios the antibiotic proved to be an effective agent in the treatment of experimental cholera. The effective dose was 0.5 to 2.0 mg. Although this may suggest the use of Chloromycetin in human cholera treatment the authors pointed out that it is not possible to reproduce the human disease in laboratory animals. The vomiting, diarrhea, and extreme dehydration characteristic of cholera in man is lacking in animals.

Vitamin E Control In Juvenile St. Vitus's Dance

Seventeen children with St. Vitus's dance were given 90 to 225 mg. of alpha-tocopherol a day in divided doses while 18 children were given placebos identical in appearance. In the treated group all of the patients exhibited symptomatic improvement while only 2 in the control group improved. However, Dr. G. C. Dowd reported before the recent International Conference on Vitamin E held in New York that when the control group was placed on vitamin E therapy all were symptom-free in 3 to 5 weeks.

Adrenal Cortex Hormone Causes Remission On Rheumatoid Arthritis

An adrenal cortex hormone known chemically as 17-hydroxy-11-dehydrocorticosterone and commonly as Compound E, has been used in 14 cases of rheumatoid arthritis. The hormone has proven to be highly effective in causing a remission of the symptoms of rheumatoid arthritis. However, a report by Kendall, Hench, Slocum, and Polley covered by *Drug Trade News* (24:33 (May 2, 1949)) emphasizes that it is not a cure. The pos-

—Continued on page 56a

in arthritis

- *unlike gold and other drugs*

safe detoxifying colloidal sulfur

- *relieves pain*
- *reduces joint swelling*
- *produces clinical remission even in the most severe cases*

Sulphocol® *colloidal sulfur compound*

ORAL AND PARENTERAL

Sulphocol Capsules (5 gr.) 1 or 2 after meals. Bottles of 100. Sulphocol Sol (parenteral), 25 cc. vials; 12 and 100-2 cc. vials. 1/4 to 1/2 cc. intramuscularly at 3 to 7 day intervals, gradually increased to 3 cc. Write for literature and samples of Sulphocol Capsules.

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THE NATIONAL DRUG COMPANY, PHILADELPHIA 44, PA.
Manufacturers of Pharmaceutical, Biological and Biochemical Products for the Medical Profession

MODERN THERAPEUTICS

—Continued from page 54a

sibility that rheumatoid arthritis may be due to a hormone deficiency received further support when the investigators found that adrenocorticotropic hormone obtained from the pituitary gland gave essentially the same action as Compound E against arthritis. Compound E was given in doses as high as 100 mg. a day. The substance was originally obtained from the adrenal glands of cattle but is now being manufactured synthetically.

Antihistamine Therapy of Bee Stings

Stings of bees, wasps and ants produce harmful effects on humans ranging from slight local pain or discomfort to a shock-like condition or death.

Investigation by Strauss, *J.A.M.A. (140:* 603 (June 18, 1949)), has shown that allergy is probably a factor in the human response to bee stings. The addition of a very small amount of bee venom to a bath containing guinea pig uterine muscle produces a distinct histamine-like reaction.

Because of the probable presence of histamine in bee venom, Thephorin, an antihistamine of proved clinical value, was applied in 5 percent ointment form to bee stings. "In every instance the pain and stinging sensation was relieved within one or two minutes," and most patients experienced no local swelling. No side effects from the drug were observed.

The author believes Thephorin ointment is the treatment of choice for bee stings and that "there is no longer any place for outmoded forms of therapy for insect bites and stings."

Undecylenic Acid Therapy In Arthritis

Perlman reported that the oral administration of 1 to 2.5 Gm. of undecylenic acid three times a day to 6 patients, 4 with arthritis and 2 with bursitis, resulted in a reduction in pain within one-week. In 3 of the patients the subcutan-

—Continued on page 58a

AN APPROVED TECHNIQUE

JUST OFF THE PRESS - -

IMPROVED METHOD OF CONTRACEPTION—a twelve-page brochure with five full-color anatomical illustrations—presents a complete description of the improved diaphragm and jelly method of contraception, which, according to the A.M.A. Council on Pharmacy and Chemistry, offers a maximal degree of protection.

The brochure features an improvement in contraceptive technique designed to give greater protection by assuring an adequate supply of spermatocidal jelly around the cervix, where it is needed most.

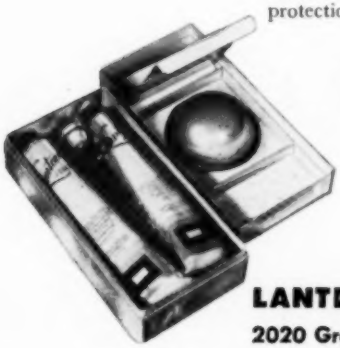
Available Without Cost to the Medical Profession

On request, Lanteen Medical Laboratories will send without charge:

1. The brochure, "Improved Method of Contraception."
2. The full-size professional package of Lanteen Jelly.

The unusually fine quality and construction of the Lanteen Diaphragm and the rapidly spermatocidal action and soothing effect of Lanteen Jelly are the basis for the safe and effective protection afforded by the IMPROVED METHOD OF CONTRACEPTION.

Lanteen Jelly contains: Ricinoleic Acid, 0.50%; Hexylresorcinol, 0.10%; Chlorothymol, 0.0077%; Sodium Benzoate and Glycerine in a Tragacanth base.



The Lanteen Diaphragm and Lanteen Jelly are accepted by the Council on Physical Medicine and the Council on Pharmacy and Chemistry of the American Medical Association, respectively.

Lanteen

LANTEEN MEDICAL LABORATORIES, INC.

2020 Greenwood Street, Evanston, Ill.

MODERN THERAPEUTICS

—Continued from page 56a

eous nodules became smaller and less painful and the swelling and pain in the joints became greatly reduced. Writing in *Urol. and Cutan. Rev.* (53:103 (1949)) the author stated that most of these patients had previously been unsuccessfully treated with salicylates, diathermy, and gold injections.

Therapy of the Common Cold With Antihistaminics

It is believed that the common cold is an allergic reaction because of its similarity symptomatically to hay fever and also to the phenomenal cure of very early colds with the antihistaminics. Benadryl, Pyribenzamine, Neoantergan, Thenylene, and Histadyl were the antihistaminic drugs used by Brewster in a study reported in the *U. S. Naval Med. Bull.* (49:1 (Jan.-Feb. 1949)). All were effective but Neoantergan produced little or no sedative effect and was thus the favorite among the patients. The dose for adults was set at 50 mg. for the antihistaminics and 16 mg. each for codeine sulfate and papaverine hydrochloride. The latter combination was given to the patients used as controls. The patients were instructed to repeat the dose every 4 hours for at least 3 doses, and for more if the symptoms persisted.

In a series of 572 patients with common colds it was found that the effectiveness of treatment is inversely proportional to the lapse of time between the onset of symptoms and the beginning of therapy. When treatment with the antihistaminics was begun within the first hour after the onset of symptoms 19 of 21 were cured, after 2 hours 48 of 55 were cured, within 6 hours 116 of 156 were cured, and within 12 hours 165 of 234 were cured. There were 77 patients used as controls. Among the controls 14 of the 34 who received treatment within 12 hours were cured. There were no instances of severe reactions or toxemia. Drowsiness was felt by most

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of those receiving the antihistaminics. This was readily controlled by the administration of 2.5 to 10 mg. of amphetamine. The author concludes that if properly and universally used the antihistaminics could reduce the incidence of colds to near the vanishing point.

Plastic Film Base

The requirements for plastic films vary with the specific requirements of the therapy for which the film is to be used. In most cases the films should be transparent so that healing may be observed; it should be elastic but also tough so that it will be long-lasting; it should set quickly when applied so that it will remain in the desired position; it should form a nonporous film over the area to prevent contamination and infection; its pH should be suitable for application to the skin; it should be unaffected by oils, greases and fats and should be so that the film could be made water-resistant if desired; and the medication should be in a uniform suspension or solution and should be released slowly and steadily. Huston, Riedel, Murray, and Groves, writing in *Canadian Pharm. J.* (*82*:151 (Feb. 15, 1949)), state that their preliminary experiments were designed primarily toward developing a base or bases with desirable properties rather than one which would have a wide range of compatibility with medicaments, desirable though that would be.

The authors reached certain conclusions relative to the effect on the properties of bases by certain substances. Polyvinyl alcohol was found to produce the most satisfactory film relative to elasticity and transparency. Films produced with methyl cellulose are lighter, more porous and less elastic than polyvinyl alcohol films. Borax solutions cause polyvinyl alcohol films to set almost immediately while methyl cellulose along with polyvinyl alcohol increases the viscosity. Plasticizers were

—Continued on page 62a

Further Clinical Results with Undecylenic Acid in Psoriasis

New series of cases treated with Declid Capsules

● Oral administration of undecylenic acid in psoriasis, first reported from a private practice series,[1] is further scrutinized in a second publication[2] dealing with a series of clinic cases.

Forty cases which had proved refractory to other therapy were treated exclusively with undecylenic acid (Declid Capsules), for a period of 2 to 27 weeks.

Degrees of Improvement

Twelve patients (30%) were "Improved;" 15 (37%) were "Somewhat Improved;" 10 (25%) were "Unchanged;" (7%) were "Worse."

"Improved" designated very substantial degrees of recovery; "Somewhat Improved" meant less impressive, though distinct improvement. In some cases, regression preceded favorable response. No serious or lasting toxic effects were observed.

Tolerability

Declid Undecylenic Acid Capsules have been given in large daily doses over long periods without toxic symptoms or significant side reactions.

Some patients report a bitter taste, mild nausea, or belching. These are relieved by antacids. Increased bowel activity is sometimes noted. When justified, reduced dosage or temporary cessation is advised. These side effects, in most cases, do not appear when full dosage is resumed.

Dosage

Uniform or immediate response should not be expected. In each case, the dosage should be adjusted to the individual patient's response. Higher dosages generally produce proportionately greater effect.

The capsules may be taken between meals, after eating, or with food, as best tolerated by the patient. Suggested dosages:

First Week: Four Declid Capsules 3 times daily. This dosage may be continued if response is satisfactory.

Second Week: Six Declid Capsules 3 times daily, if needed.

After Second Week: 8 to 10 Declid Capsules 3 times daily if needed, and continued until complete disappearance of lesions.

Tolerability is enhanced by taking capsules with a carbonated beverage.

Adjunctive Therapy

When response to undecylenic acid therapy is slow, the conventional psoriasis treatments can be useful adjuncts. Low fat diets and topical applications may accelerate results.

Contraindications

Oral therapy with Declid Undecylenic Acid is new. Much is still unknown about its effect on metabolism. It should not be given to debilitated, diabetic or hypertensive patients, or those with coronary or gall bladder symptoms.

Declid Undecylenic Acid Capsules are to be dispensed only by or on the prescription of a physician. Supplied in Bottles of 100 or 1,000 Capsules, 0.44 gram each. Complete literature on request.

REFERENCES

1. Perlman, H. H.: Undecylenic Acid Given Orally in Psoriasis and Neurodermatitis, J.A.M.A. 139:444 (Feb. 12) 1949.
2. Perlman, H. H., and Milberg, I. L.: Peroral Administration of Undecylenic Acid in Psoriasis, J.A.M.A. 140:865 (July 9) 1949.

Declid Undecylenic Acid

DECYL PHARMACAL CO. *Distributors*
PRINCETON, N. J.

MODERN THERAPEUTICS

—Continued from page 60a

found to increase the pliability of the films but also to increase the drying time. The films dry in 10 to 15 minutes and were suitable vehicles for 1 per cent sulfathiazole. Two of the more satisfactory formulas were:

Propylene glycol	5.9
Castor oil	2.0
Polyvinyl alcohol (5 per cent) q.s	100.0
Triethanolamine	2.0
Hexaethylene glycol	4.0
Borax solution (0.5 per cent)	10.0
Polyvinyl alcohol (4 per cent) q.s	100.0

Aureomycin Therapy In Human Brucellosis

A study of the treatment of human brucellosis caused by the more malignant strain *Brucella melitensis* has shown that aureomycin is more effective in the control of the disease than is the combination of streptomycin and sulfadiazine. The results obtained clinically far surpassed expectations based upon *in vitro* and chick embryo tests. The use of aureomycin was brought about by the lack of hospital beds in the highly endemic area of Mexico where the study was made. Since aureomycin is administered orally the patients can remain ambulatory, according to Spink, Braude, Castaneda, and Goytia in *J.A.M.A. (138*:1145 (Dec. 18, 1948)). The treatment recommended consisted in an initial dose of 0.1 Gm. in 4 divided doses the first day, 0.6 Gm. the second day, 1.6 Gm. the third day, and 2 Gm. the fourth day and for succeeding days until the drug has been given for 10 days. The initial dose was small because it was found that larger initial doses caused a febrile reaction associated with a drop in blood pressure, in many instances. An addendum to the original article reported that of 24 patients treated 3 had shown positive blood cultures within 3 months after treatment. Therefore, the authors recommended that

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MODERN THERAPEUTICS

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the dose be increased from 2 Gm. to 4 to 6 Gm. for 2 weeks. The authors also emphasized that this was a preliminary report based upon immediate therapeutic results and that in a disease such as brucellosis a long follow-up period is necessary in order to properly evaluate the drug.

Bacterial Resistance Lessened With Internal Administration Of Streptomycin

The administration of streptomycin at intervals of 3, 4 or 5 days seems to defer the development of bacterial fastness to the antibiotic. A study of 16 cases of tuberculosis was reported by Deyke, Fisher, James, and Sides in *Ann. Int. Med.* (*34*: 619 (1949)). All were given streptomycin in 5 divided doses totalling 2 Gm. a day, on the day therapy was given. Eight patients received therapy every third day, one every fourth day, and seven every fifth day. All were positive bacteriologically before therapy was begun. Roentgen studies were made throughout the study and cultures were taken weekly. All positive cultures were tested for sensitivity. In eight cases the bacteria were converted to other strains, in one they developed resistance to streptomycin, and in 7 the tubercle bacilli remained sensitive to the antibiotic. An addendum to the report was of interest in that 100 patients were treated every third day similar to above, and the results appeared to confirm the finding that bacterial sensitivity is prolonged when the streptomycin is administered at intervals.

Vitamin P Effect On Diabetic Retinopathy

Hesperidin methyl chalcone (vitamin P) was given to 22 patients with diabetic retinopathy in gradually increasing doses for 4 to 32 months. The patients finally received between 100 and 300 mg. a day. Peck and Mann reported in *Am. J. Med. Sci.* (*217*:277 (1949)) that 5 of the patients showed improvement, in 5 the lesions remained stationary, in 6 there was a definite increase in retinal hemorrhages

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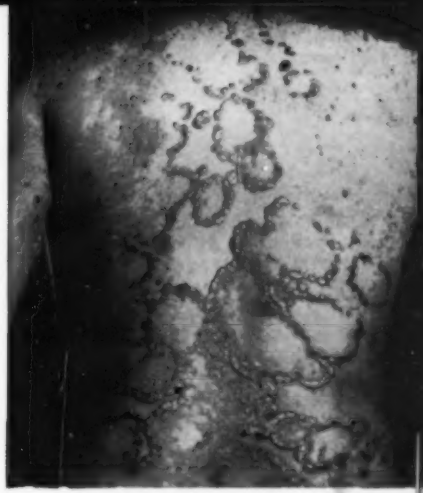
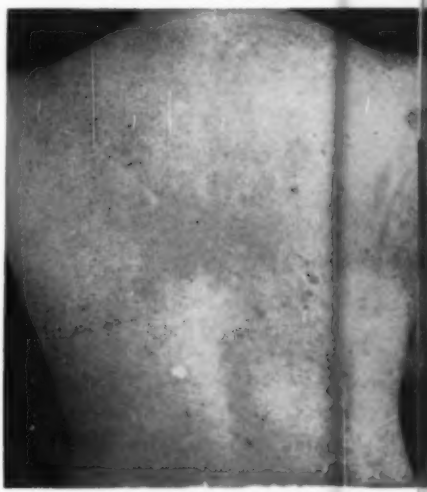
PSORIASIS
Etiology Unknown

treatment

RIASOL



Before Use of RIASOL



After Use of RIASOL

Since the etiology of psoriasis is unknown, there is a logical basis for palliative treatment with RIASOL. Abundant clinical observations have established the superior efficacy of local treatment with a mercurial chemically combined with soaps.

Thousands of physicians all over the United States are treating psoriasis with RIASOL. Their own experience is the best proof of its value for removing the local lesions and minimizing their recurrence. RIASOL is simple, pleasant and convenient to use.

RIASOL contains 0.45% mercury chemically combined with soaps, 0.5% phenol and 0.75% cresol in a washable, non-staining, odorless vehicle.

Apply daily after a mild soap bath and thorough drying. A thin, invisible, economical film suffices. No bandages necessary. After one week, adjust to patient's progress.

RIASOL is ethically promoted. Supplied in 4 and 8 fld. oz. bottles at pharmacies or direct.

Mail coupon today for your free clinical package. Prove RIASOL in your own practice.

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RIASOL for PSORIASIS

MODERN THERAPEUTICS

—Continued from page 64a

during treatment, and in 6 there was no evident correlation between the therapy and the course of retinopathy.

Synthetic Anti-Clotting Agent May Rival Heparin

A comparatively inexpensive anti-clotting agent which may rival heparin in the treatment of coronary thrombosis, pulmonary emboli, thrombophlebitis, and other diseases which are associated with blood clotting has been named Paritol. It is a sulfated mannuronic acid and has about the same molecular and particle size as heparin. According to a release date June 2, 1949 the drug has been tested on animals and a total of 25 injections have been made intravenously in human patients. The amount of the synthetic drug required to prolong the clotting time is about 10 times as large as is required using heparin but the action lasts twice as long. The side reactions which have been noted have cleared spontaneously or have responded promptly to administration of epinephrine.

NEWS AND NOTES

Gift of $13,000 to U. of Illinois Epilepsy Clinic

The Junior League of Chicago has awarded a gift in the amount of $13,000 to the University of Illinois Research and Educational Hospitals for the purpose of maintaining and operating the Consultation Clinic for Epilepsy. The gift covers a period of one year. It represents the continuation of support of the clinic by the Junior League. More than 1,000 patients have been seen in the clinic since it was established in 1946. Support for the clinic also has been provided by the Division of Rehabilitation of the State Department of Public Welfare, and the Division of Special Services for Crippled Children. Dr. Frederic A. Gibbs is director of the clinic.

Symposium on Inhalational Therapy

The Committee on Public Health Relations of The New York Academy of Medicine is to present a Symposium on Inhalational Therapy, consisting of exhibits, demonstrations, motion pictures and lectures at the Academy building, 2 East One Hundred and Third Street, New York City, December 5 to 10, inclusive. The purpose of this event is to bring to physicians interested in this field, as well as to hospital administrators, resident staffs and nurses, information as to recent developments in this aspect of therapy and the efficient use of the equipment available for it.

Grant Of $15,000 To Ill. Coll. of Med.

The U. S. Public Health Service has awarded a grant in the amount of $15,000 to the University of Illinois College of Medicine in support of research studies involving the 22-million volt betatron.

The grant will be used specifically for the study of the effects of the betatron x-ray beam on bone and cartilage. The study is under the supervision of Dr. Roger A. Harvey of the department of radiology and Dr. G. A. Bennett of the department of pathology.

Risks Are Involved In Use of Many Hair Dyes

Unfavorable reactions to certain hair dyes may be due to a sensitivity which could not be predicted by present methods, says a report of the American Medical Association Committee on Cosmetics in a recent issue of Hygeia.

Dyes should never be used on a scalp that has breaks in the skin and should never be permitted to get into the eyes, the committee advises.

Henna and other dyes of vegetable origin are among the safest preparations for hair coloring. Few cases of sensitivity due to their use have been reported.

Reactions to hair dyes are most often characterized by a rash of the scalp, face, and neck. A few have been reported to have caused generalized skin disturbances, disturbances of the eyes, neuralgic pain, headaches, and other complaints.

Metallic hair dyes create the illusion that color is being restored to the hair and have been called "hair color restorers" rather than dyes. Laboratory and clinical evidence indicates that the metallic salts that make up these dyes are not absorbed through the skin. But if they should enter the blood stream through scalp lesions or through contamination of food by hands which are not washed thoroughly after use of the dye, the chemical may accumulate in the body and eventually cause symptoms of metallic poisoning, the committee says.

—Continued on following page

NEWS AND NOTES

—Continued from preceding page

Rimless Spectacles May Cause Cancer Of Face

Rimless spectacles that focus light on the face may cause cancer, according to four doctors from the Department of Dermatology, Jefferson Medical College, Philadelphia.

Twelve cases in which skin conditions near the eyes were believed to have been caused by the heat or chemical rays conducted by spectacle lenses are reported by Drs. Edward F. Corson, George M. Knoll, Herbert A. Luscombe, and Henry B. Decker in a recent issue of Archives of Dermatology and Syphilology, published by the American Medical Association.

In nine of these patients the condition was diagnosed as cancer, and in another patient as keratoses, premalignant growths caused by radiation. The remaining two patients were believed to have chronic actinic dermatitis, a skin disturbance caused by light rays. All the patients were white. The doctors say they have not observed similar conditions in Negroes.

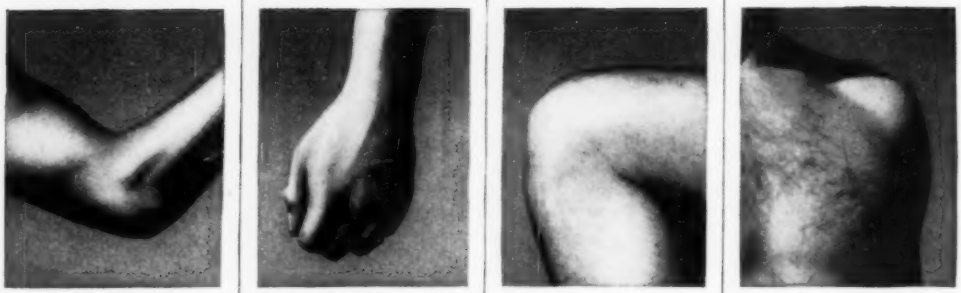
"In our investigations it was found that certain types of spectacle frames were especially responsible for transmission of light and its focusing on the skin below the lower edge of the lens," the doctors explain. "These were, above all, the rimless spectacles with lenses of round or elliptic [oval] outline.

"While the character of the lens—whether thick or thin, sphere, cylinder, or prism—was responsible for a certain difference, the same principle existed in all cases in which a wholly or partially unobstructed rim of the lens was present.

"The route traversed by the light beam could be blocked readily at either edge by the use of a lacquer employed by the optical trade and known as rim black. When carefully applied either to the upper or the lower rim of the lens it was hardly noticeable and the rays we deemed important in their effects on the skin were entirely cut off."

MEDICAL (advertisers index) TIMES
NOVEMBER, 1949

Beyond the reach of human fingers



Beneficial effects may be exerted, not just locally but systemically, "beyond the reach of human fingers" in such conditions as arthritis, myositis, muscle sprains, bursitis and arthralgia. That systemic as well as local effects may be achieved by such preparations as Baume Bengué was conclusively demonstrated by the fundamental work of Moncorps, Kionka, Hanzlik, Brown and Scott.

LOCALLY — *at the site of discomfort analgesic relief and a beneficial hyperemia may be readily induced.*

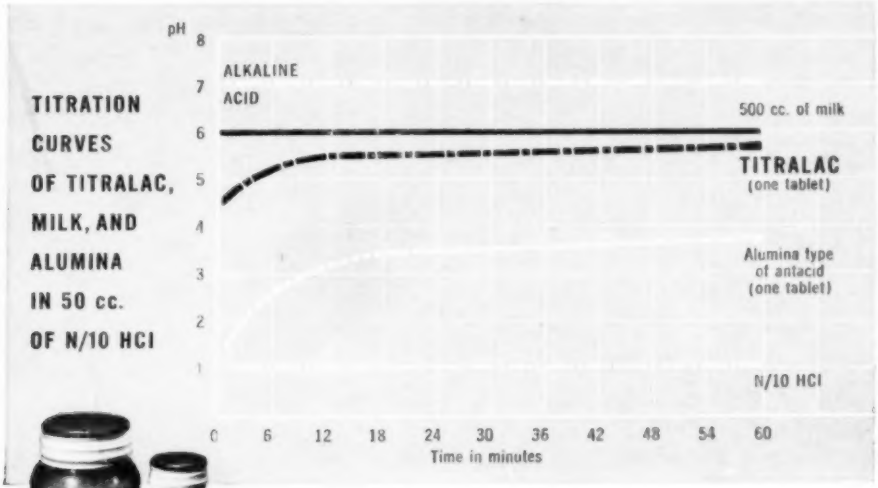
SYSTEMICALLY — *the salicylate absorption promoted by Baume Bengué's methyl salicylate concentration produces systemic effects to reinforce other indicated therapeutic measures.*

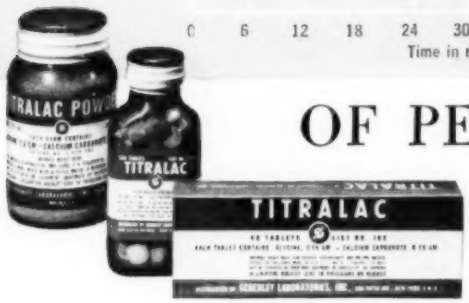
Baume Bengué provides 19.7% *methyl salicylate,* 14.4% *menthol in a specially prepared lanolin base.*

Baume Bengué ANALGÉSIQUE

THOS. LEEMING & CO., INC., 155 E. 44th ST., NEW YORK 17, N. Y.

NON-SURGICAL TREATMENT





OF PEPTIC ULCER

Gastroenterologists have long endorsed the use of milk, when practicable, for its ideal acid-converting power and buffering capacity.[1, 2] In a recent comprehensive paper, Aaron[3] and others[4, 5, 6] express a preference for calcium carbonate as the antacid to be employed.

TITRALAC, by combining proper proportions of purified calcium carbonate and the amino acid glycine, *provides an acid-converting and buffering effect practically equivalent to that of fresh milk*, as shown in the above chart.* Just 1 TITRALAC tablet is equivalent to an 8-ounce glass of milk in antacid effect and provides quick and long-lasting relief from the distressing symptoms of hyperacidity.

The very agreeable taste of soft-massed TITRALAC tablets, which is achieved without employing taste-disguising, acid-generating sugars in the formula, makes them as acceptable to patients as an after-dinner mint. Prescribing TITRALAC eliminates the probability of unfavorable reactions often associated with the taking of metallic-tasting, astringent tablets or liquids, and ensures adherence to the prescribed dosage.

TITRALAC tablets are supplied in bottles of 100 and convenient-to-carry packages of 40. TITRALAC powder is also available, in 4-oz. jars.

REFERENCES

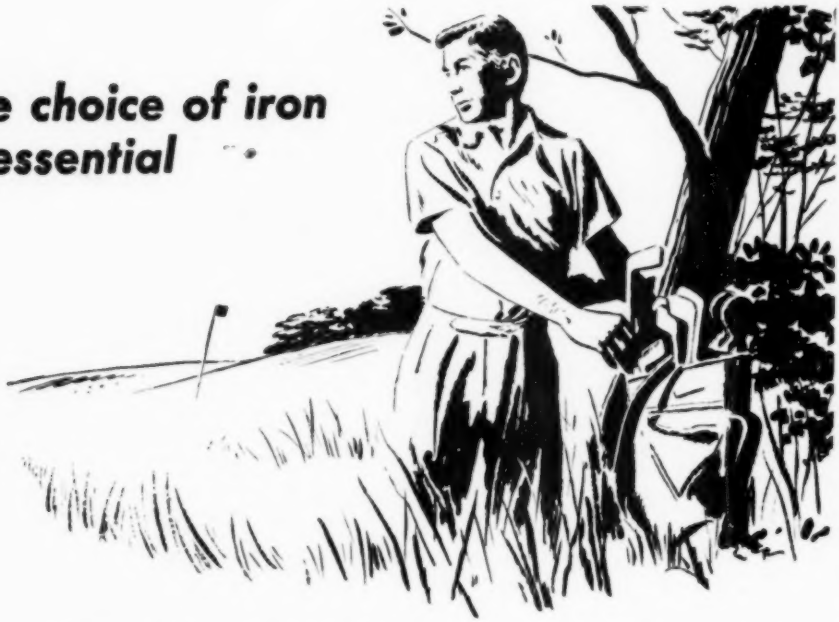
1. Rossett, N. E., and Flexner, J.: Ann. Int. Med. 18: 193 (1944). 2. Freezer, C. R. E.; Gibson, C. S., and Matthews, E.: Guy's Hosp. Reports 78: 191 (1928). 3. Aaron, A. H.; Lipp, W. F., and Milch, E.: J. A. M. A. 139: 514 (Feb. 19) 1949. 4. Kirsner, J. B., and Palmer, W. L.: Illinois M. J. 94: 357 (Dec.) 1948. 5. Kimball, S.: in Practice of Medicine (Tice). Hagerstown, Md., W. F. Prior Company, Inc., 1948; p. 210. 6. Special Article: M. Times 76: 10 (Jan.) 1948.

* The formula of TITRALAC is one whose composition and mode of action are recognized by U.S. Patent No. 2,429,596.

Samples and literature to physicians upon request.

SCHENLEY LABORATORIES, INC., 350 FIFTH AVENUE, NEW YORK 1, N. Y.

The choice of iron is essential



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ADULTS: One tablespoonful 3 or 4 times daily in water or milk.
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